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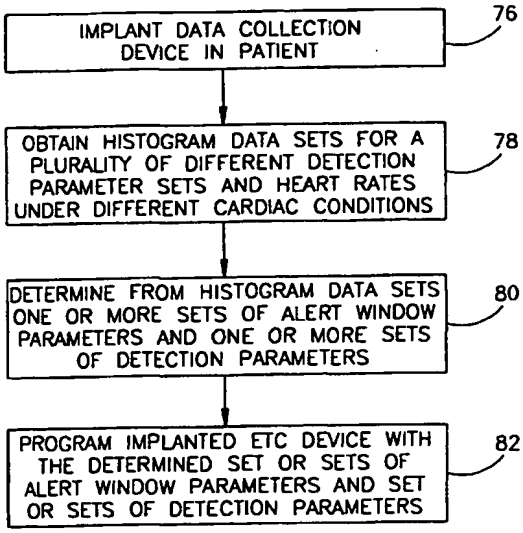


(57) Abstract: Apparatus and method for obtaining from a patient's heart data useful for on-line setting of the parameters of a detection time window in an excitable tissue control device. The method includes applying electrodes to a first cardiac site and a second cardiac site of a patient and electrically connecting the electrodes to a data collecting device. The device is then operated under a plurality of different cardiac conditions to obtain a plurality of different histogram data sets. Each histogram data set represents a cumulative time distribution histogram of cardiac depolarization events detected at the second cardiac site in a plurality of cardiac beats. Each histogram data set is defined by a plurality of histogram parameters having values indicative of the cardiac conditions common to the plurality of cardiac beats used to obtain the histogram data set. The histogram parameters include a sensitivity level parameter representing the sensitivity level used for detecting the cardiac depolarization events of the plurality of cardiac beats at the second cardiac site. Another histogram parameter represents the range of values of the beat to beat time interval for the beats who's data is included in the histogram data set. Another histogram parameter has values indicating if the beats who's data is included in the histogram data set were acquired under conditions in which the delivery of non-excitatory ETC signals substantially affected or did not substantially affect the velocity of propagation of depolarization waves in the myocardium. Another histogram parameter, which may be used in devices having pacing capability has values indicating whether the beats who's data is included in the histogram data set are paced beats or non-paced beats. The histogram data sets are processed for computing a set of data usable for on-line setting of the parameters of a detection time window. This set of data may then be used for operating an implanted or external ETC device operatively connected to the electrodes.

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# APPARATUS AND METHOD FOR COLLECTING DATA USEFUL FOR DETERMINING THE PARAMETERS OF AN ALERT WINDOW FOR TIMING DELIVERY OF ETC SIGNALS TO A HEART UNDER VARYING CARDIAC CONDITIONS

## FIELD OF THE INVENTION

The present invention relates generally to the field of methods and medical devices for cardiac pacing and for modulating cardiac muscle activity and contractility and more specifically to the field of methods for determining timing of delivery of excitable tissue controller (ETC) signals under a variety of conditions including varying heart rates, paced or sensed triggering and the absence and presence of ETC signals.

## BACKGROUND OF THE INVENTION

Excitable tissue controllers (ETCs) are devices which modulate the activity of excitable tissues by application of non-excitatory electrical stimulation to the excitable tissue through suitable electrodes in contact with the tissue. For example, ETC devices may be used, *inter alia*, to increase or decrease the contractility of cardiac muscle *in vitro*, *in vivo* and *in situ*., as disclosed in detail in PCT application, International Publication Number WO 97/25098 to Ben-Haim et al., titled "ELECTRICAL MUSCLE CONTROLLER". Other methods and applications of ETC devices are disclosed in PCT applications commonly-assigned to the assignee of the present application, International Publication Number WO 98/10828, titled "APPARATUS AND METHOD FOR CONTROLLING THE CONTRACTILITY OF MUSCLES" to Ben Haim et al., International Publication Number WO 98/10829, titled "DRUG-DEVICE COMBINATION FOR CONTROLLING THE CONTRACTILITY OF MUSCLES" to Ben Haim et al., and International Publication Number WO 98/10830, titled

"FENCING OF CARDIAC MUSCLES" to Ben Haim et al., incorporated herein by reference, International Publications Number WO 98/10831 to Ben Haim et al., titled "CARDIAC OUTPUT CONTROLLER".

Further applications of the ETC including devices combining cardiac pacing and cardiac contractility modulation are disclosed in PCT Application, International Publication No. WO 98/10832, titled "CARDIAC OUTPUT ENHANCED PACEMAKER" to Ben Haim et al., co-assigned to the assignee of the present application. Such ETC devices function by applying non-excitatory electrical field signals of suitable amplitude and waveform, appropriately timed with respect to the heart's intrinsic electrical activity to selected cardiac segments. The contraction of the selected segments can be modulated to increase or decrease the stroke volume of the heart. The timing of the ETC signals must be carefully controlled since application of the ETC signal to the myocardium at inappropriate times may be arrhythmogenic. The ETC signals must therefore be applied to the selected cardiac segment within a defined time interval during which the selected cardiac segment will not be stimulated by the ETC signals.

As disclosed in International Publication No. WO 98/10832, the ETC signals may be timed relative to a trigger signal which is also used as a pacing trigger, or may be timed relative to locally sensed electrogram signals.

International Application No. PCT/IL00/00126 Titled "APPARATUS AND METHOD FOR TIMING THE DELIVERY OF NON-EXCITATORY ETC SIGNALS TO A HEART", discloses a method for timing the delivery of non-excitatory ETC signals to a heart using, inter alia, an alert window period for reducing the probability of delivering an improperly timed ETC signal to the heart due to spurious detection of noise or ectopic beats.

The methods of timing of the delivery of ETC signals disclosed hereinabove do not take into account the fact that naturally occurring and pacemaker induced changes in heart rate (HR) may cause changes in the velocity of propagation of the depolarization wave in the myocardium. Additionally, the delivery of the ETC signals to the myocardium may also cause changes in the velocity of propagation of the depolarization wave in the

myocardium. Other factors such as, *inter alia*, various cardio-active drug treatments and myocardial pathological conditions such as ischemia may also cause changes in the velocity of propagation of the depolarization wave in the myocardium. It is therefore desirable to have a method for determining proper timing of the delivery of ETC signals which takes into account variations in velocity of propagation of the depolarization wave in the myocardium under different cardiac conditions.

## SUMMARY OF THE INVENTION

Accordingly, it is an object of the present invention to provide apparatus and methods for obtaining data from a heart of a patient. The obtained data is useful for on-line determining of the parameters of a detection time window. The detection time window is used in an ETC device to detect depolarization events for triggering the application of non-excitatory ETC signals to the heart of the patient. The detection time window is also referred to as the "alert time window" or "alert window" hereinafter.

A feature of the present invention is the applying of electrodes to a first cardiac site and a second cardiac site of the patient. The electrodes are operatively connected to a data collection device. In accordance with one preferred embodiment of the present invention the first cardiac site is in or about the right ventricle of the heart and the second cardiac site is in or about the left ventricle of the heart. In accordance with another preferred embodiment of the present invention the first cardiac site is in or about the right atrium of the heart and the second cardiac site is in or about the left ventricle of the heart.

In accordance with a preferred embodiment of the present invention, the device has circuitry adapted for sensing and detecting cardiac depolarization events using one or more of the applied electrodes and for delivering non-excitatory ETC signals to the heart. In accordance with another preferred embodiment of the present invention, the device may also include circuitry for delivering pacing pulses to one or more sites of the patients heart.

Another feature of the present invention is the triggering of a data collection time interval for detecting depolarization events at the second cardiac site. In accordance with one preferred embodiment of the present invention, the data collection time interval is triggered by the detection of a depolarization event at the first cardiac site. In accordance with another preferred embodiment of the present invention, in a device capable of delivering pacing pulses to the heart, the data collection time interval is triggered by the detection of a depolarization event at the first cardiac site or by the delivery of a pacing pulse to the first cardiac site.

The data collection time interval is virtually divided into a plurality of contiguous time bins. All of the time bins have an identical duration which is smaller than the duration of the data collection time interval.

The data collection device includes a memory for storing a plurality of histogram data sets. Each of the histogram data sets is stored in the memory of the device as a separate data structure including a plurality of data elements. Each of the data elements of a histogram data set is associated with a single time bin of the data collection interval. The number of time bins is identical to the number of data elements included in any of the data histogram sets. The value stored in each of the data elements is an integer number representing the cumulative number of depolarization events detected within the time bin associated with the data element at said second cardiac site in a plurality of cardiac beats.

Each of the plurality of the histogram data sets represents a cumulative time distribution histogram of cardiac depolarization events detected at said second cardiac site in a plurality of cardiac beats.

Each histogram data set is associated with a plurality of histogram parameters. The histogram parameters have values indicative of the cardiac conditions common to the plurality of cardiac beats used to obtain the histogram data set. The histogram parameters include a sensitivity level parameter having a value indicative of the detection sensitivity level used for detecting the cardiac depolarization events of the plurality of cardiac beats used for acquiring the data of the histogram.

Typically, the data is acquired by recording data from a plurality of cardiac beats under a variety of different cardiac conditions. The beat's cardiac conditions may include beats induced by natural pacing of an intrinsic cardiac pacemaker such as the heart's sino-atrial node (referred to as sensed beats), beats induced by delivering an artificial pacing pulse to the heart (referred to as paced beats), beats for which prior application of ETC signals to the heart has induced a substantial change in the velocity of propagation of a depolarization wave in a part of the myocardium and beats for which prior application of ETC signals to the heart has not induced a substantial change in the velocity of

propagation of a depolarization wave in a part of the myocardium. The cardiac conditions also include the cycle length of the beats which is the beat to beat time interval as obtained from the measured R-R interval or A-A interval depending on the choice of the first cardiac site. All the beats used for obtaining a specific histogram data set have a beat cycle length which is within a certain range of cycle lengths associated with that specific histogram data set. Each of the histogram data sets is also associated with a particular detection sensitivity level which was used for detecting of the depolarization events at the second cardiac site during the data collection time interval of each of the beats which are sampled for the histogram data set.

The histogram data sets may be collected in the patient during a data acquisition period in which the patient may perform a regime which includes certain physical exercise types top ensure that a sufficient number of beats are sampled for a suitable range of heart rates. If the data collecting device includes pacing capabilities, the A-V delay of the pacing circuitry may be varied manually or automatically to ensure a desired ratio of paced to sensed beats.

After the histogram data sets are acquired, they may be telemetrically or non-telemetrically transferred to an analyzing unit for processing. The analyzing unit may be a separate device external to the patient or may be part of a data collection device which is disposed outside of the patient. The histogram data sets are processed to provide a plurality of sets of alert window parameters which are found to yield a desired level of event detection. The plurality of sets of alert window parameters may be programmed as an array or look up table (LUT) into an ETC device or pacemaker/ETC device such as the data collection device which is already implanted within the patient. If the data collection device is an external device disposed outside the patient, the array or LUT may be programmed into an ETC device or pacemaker/ETC device after they are connected to the electrodes and implanted in the patient. Each of the plurality of sets of alert window parameters may include a starting bin number and an ending bin number (in which case the array or LUT also includes the value of the bin duration for enabling on-line computation of the beginning and ending time points of the alert window) which are associated with a particular unique

combination of cardiac condition parameters. Alternatively, each of the plurality of sets of alert window parameters may include a starting time and an ending time for the alert window which are associated with a particular unique combination of cardiac condition parameters.

The plurality of sets of alert window parameters may be further processed to derive a set of approximation parameters which may be used for computing of approximated alert window parameters which are corrected to account for the actual measured beat cycle length. The set of approximation parameters may be programmed as an array or look up table (LUT) into the ETC device or the pacemaker/ETC device. The approximation parameters may be computed using piece-wise linear approximation methods or other suitable approximation methods.

In accordance with a preferred embodiment of the present invention, the alert window parameter sets may also be in a partially degenerate form in that some or all of the parameters may have a single value for all the cardiac conditions. For example, if no pacing is performed by the data collection device, the values of the condition parameters associated with all the sets of approximation parameters are degenerate since they only have a value indicative of the beats being sensed beats and may not assume the value indicative of paced beats.

Another feature of the present invention is that the array or LUT which is obtained by processing the histogram data sets may also include a plurality of sets of detection sensitivity level parameters. Each set of detection sensitivity level parameters may include one or more parameters for on-line determination of the detection sensitivity level based on the current cardiac conditions. The number and type of the detection sensitivity level parameters depends on the detection method that was used in collecting the histogram data sets. For example, in accordance with one preferred embodiment of the present invention, event detection is performed by using a single positive threshold crossing criterion. In such a case, each set of detection sensitivity level parameters includes a single threshold value associated with a specific set of

cardiac condition parameters. This single threshold value represents the threshold level to be used by the ETC device or pacemaker/ETC device of the patient under the cardiac conditions. Other event detection methods may also be used such as, but not limited to, morphological detection methods or combined slope and threshold methods. If such other detection methods are used, each set of detection sensitivity level parameters may include one or more detection sensitivity level parameters, depending on the particular event detection method used.

In accordance with other preferred embodiments of the present invention, the plurality of sets of detection sensitivity level parameters may also be a degenerate set. For example, if the operator or user determines that a single detection sensitivity level may be used under all possible combinations of cardiac conditions, the detection sensitivity level parameters in all the sets of detection sensitivity level parameters in the array or LUT may have identical values.

## BRIEF DESCRIPTION OF THE DRAWINGS

The invention is herein described, by way of example only, with reference to the accompanying drawings, in which like components are designated by like reference numerals, wherein:

Fig. 1 is a schematic diagram representing a typical lead placement configuration of a pacemaker/ETC device within the heart, in accordance with a preferred embodiment of the present invention;

Fig. 2 is a schematic diagram useful in understanding a method using an alert window for timing the delivery of ETC signals useful in operating the device of Fig. 1, in accordance with a preferred embodiment of the present invention;

Fig. 3A is a schematic diagram illustrating a system for determining and programming alert window parameters for an implanted ETC device or pacemaker/ETC device, in accordance with a preferred embodiment of the present invention;

Fig. 3B is schematic functional block diagram illustrating the details of an implantable device for pacing the heart, for delivering ETC signals to the heart and for data acquisition and processing usable as the implantable device of the system of Fig. 3A, in accordance with a preferred embodiment of the present invention;

Fig. 4 is schematic functional block diagram illustrating the details of another implantable device for delivering ETC signals to the heart and for data acquisition and processing which is usable as the implantable device of the system of Fig. 3A, in accordance with another preferred embodiment of the present invention;

Fig. 5 is a schematic diagram illustrating a system for pacing the heart, for delivering non-excitatory ETC signals and for non-telemetrically determining and programming alert window parameters for an ETC device or pacemaker/ETC device, in accordance with another preferred embodiment of the present invention;

Fig. 6 is a schematic functional block diagram illustrating a system 70 for delivering non-excitatory ETC signals and for non-telemetrically determining

alert window parameters for use in an ETC device, in accordance with another preferred embodiment of the present invention;

Fig. 7 is a schematic diagram illustrating the structure of a typical data collection time interval useful in the acquisition of data histograms, in accordance with a preferred embodiment of the present invention;

Fig. 8A is a schematic diagram illustrating the general steps of a method for collecting time histogram data sets under various cardiac conditions and for determining one or more sets of alert window parameters or one or more and one or more detection parameter sets from the histogram data, in accordance with a preferred embodiment of the present invention;

Figs. 8B and 8C are schematic flow control diagrams illustrating the steps of a data collection method for collecting time histogram data sets in detail, in accordance with a preferred embodiment of the present invention;

Fig. 9 is a schematic graph illustrating a typical cumulative distribution of cardiac cycle length;

Fig. 10 is a schematic diagram illustrating the steps of the method of updating the value of the logical variable ETC of Figs. 8B-8C;

Figs. 11A and 11B are schematic control flow diagrams of the main program implementing the method for analyzing acquired data histograms, in accordance with a preferred embodiment of the present invention;

Fig. 12 is a schematic flow control diagram illustrating the steps of the sensitivity level determining procedure used in the main program of Figs. 11A-11B;

Figs. 13A–13C are schematic flow control diagrams illustrating the steps of the window position determining procedure used in Figs. 11A, 11B and in Fig. 12;

Fig. 14 is a schematic flow control diagram representing the steps of a procedure for determining the sum of the number of detected events stored in a given data histogram, in accordance with a preferred embodiment of the present invention;

Fig. 15 is a schematic flow control diagram illustrating the steps of a procedure for determining the value of a variable N usable in the window position determining procedure of Fig. 13A-13C;

Fig. 16 is a schematic flow control diagram illustrating the steps of a group sorting procedure usable in the window position determining procedure of Figs. 13A-13C, in accordance with a preferred embodiment of the present invention;

Fig. 17 is a schematic flow control diagram illustrating the steps of the group enlarging procedure usable in the window position determining procedure of Figs. 13A-13C, in accordance with a preferred embodiment of the present invention;

Fig. 18 is a schematic flow control diagram illustrating the steps of the group shrinking procedure usable in the window position determining procedure of Fig. 13B, in accordance with a preferred embodiment of the present invention;

Fig. 19 is schematic flow control diagram illustrating the steps of the common window position parameters determining procedure usable in the main data analysis program of Figs. 11A -11B, in accordance with a preferred embodiment of the present invention;

Fig. 20 is a schematic graph useful for understanding a method for computing a set of approximation parameters useful for the real time computing of the alert window parameters, in accordance with a preferred embodiment of the present invention;

Fig. 21 is a schematic flow control diagram illustrating the steps of an exemplary procedure for determining the real time window approximation parameters of Fig. 19, in accordance with one preferred embodiment of the present invention;

Fig. 22 is a schematic control flow diagram illustrating the steps of a method for real time determination of the beginning and ending time points of an alert window and of the detection parameters in an ETC device having pacing capabilities, in accordance with a preferred embodiment of the present invention;

Figs. 23A-23B are schematic flow control diagrams illustrating the steps of a method for acquiring time histogram data sets under various cardiac conditions in the absence of artificial cardiac pacing and for determining one or more sets of alert window parameters or approximation parameters and one or more detection parameter sets from the histogram data, in accordance with a preferred embodiment of the present invention; and

Fig. 24 is a schematic control flow diagram illustrating the steps of a method for real time determination of the beginning and ending time points of an alert window and of the detection parameters in a non-pacing ETC device, in accordance with another preferred embodiment of the present invention.

## DETAILED DESCRIPTION OF THE INVENTION

Notation Used Throughout

The following notation is used throughout this document.

| Term | Definition |
|---|---|
| RV | Right ventricle |
| LV | Left ventricle |
| SE | Sensed Event |
| PE | Paced Event |
| ETC | Excitable Tissue Control |
| PVC | Premature Ventricular Contraction |
| IEGM | Intra-cardiac Electrogram |
| SVC | Superior Vena Cava |
| GCV | Great Cardiac Vein |
| CS | Coronary Sinus |
| PAC | Premature Atrial Contraction |

Method of timing of ETC signal delivery

Typically, ETC signal delivery is timed relative to a sensed signal representing the depolarization wave locally sensed at or near the site of the electrodes used for ETC signal delivery. This signal may be a biphasic or polyphasic intra-cardiac electrogram (IEGM) signal sensed by a lead or catheter including one or more electrodes capable of sensing an IEGM signal and of delivering pacing pulses. The depolarization wave represented by the IEGM is an electrical event caused by spreading myocardial electrical excitation evoked by the natural pacemaker of the heart (normally the Sino-atrial node) in which case the event is referred to as a sensed event (SE), or by a pacing pulse delivered to the myocardium by, in which case the event is referred to as a paced event (PE). The IEGM signal may also include electrical depolarizations

caused by ectopic myocardial activation such as premature atrial contractions (PAC) or premature ventricular contraction (PVC). Furthermore, the IEGM signal may include artifacts caused by electrical noise.

Reference is now made to Fig. 1 which is a schematic diagram representing a typical lead placement configuration of a pacemaker/ETC device within the heart, in accordance with a preferred embodiment of the present invention. The term pacemaker/ETC device generally refers throughout the present application to a device capable of pacing a heart and of delivering non-excitatory ETC signals to the heart. The Pacemaker/ ETC device 1 includes an implantable housing or case 3 for housing the electronic circuitry 5 (not shown in detail in Fig. 1) of the device 1. A pacing/sensing lead 2 is suitably connected to the case 3 and operatively connected to the circuitry 5.

The lead 2 includes an electrode 2A applied to the right atrium (RA) 8. The electrode 2A is used for sensing SEs and for delivering pacing pulses if necessary. The left atrium 7 (LA) is also shown in Fig. 1. The pacing lead 2 may be inserted into the RA 8 through the sub-clavian vein and the superior vena cava (SVC), but other methods of insertion are also possible. Another pacing/sensing lead 4 is connected to the case 3 and operatively connected to the circuitry 5. The lead 4 includes an electrode 4A which is applied the right ventricle (RV) 9 and is used for sensing right ventricular SEs and PEs and for delivering pacing pulses if necessary. The lead 4 may be inserted into the RV through the subclavian vein and the superior vena cava (SVC), but other methods of insertion are also possible. A third lead 6 is also suitably connected to the case 3 and operatively connected to the circuitry 5. The lead 6 includes an electrode 6A which is applied to the wall of a lateral vein of the great cardiac vein (GCV) and is used for local sensing of SEs and PEs in the left ventricle (LV) 10 and for delivering non-excitatory ETC signals to the LV 10 if required.

The lead 6 may be inserted through the sub-clavian vein, passing through the SVC, the right atrium, the coronary sinus (CS) and the GCV and reaching a lateral vein of the GCV, but other methods of insertion of the leads 6 into or about the left ventricle (LV) are also possible. The implantable case 3 is typically implanted in a thoracic sub-cutaneous pocket (not shown), but other

implantation positions are also possible. It is noted that the above disclosed lead placements and insertion paths and the case placement are given by way of example only and that other electrode placements and lead insertion paths and case placements are also possible.

It is noted that while each of the single electrodes 2A, 4A and 6A of the device 1 of Fig. 1 may be used for sensing with respect to a common reference point such as the case 3 of the device 1, other preferred embodiments of the present invention may use pairs of locally applied electrodes (not shown) which may be used for local differential sensing. For example, the lead 2 may include a pair of electrodes (not shown) which are applied to the RA 8 for local sensing, the lead 4 may include a pair of electrodes (not shown) which are applied to the RV 9 for local sensing and the lead 6 may include a pair of electrodes (not shown) which are applied to the LV 10 for local sensing.

It is further noted that while the electrode 2A of the lead 2 is used for both sensing and pacing the RA 8, in other preferred embodiments of the present invention the lead 2 may include additional electrodes or electrode pairs (not shown) such that one or more electrode or electrode pair is used for sensing in the RA 8 while other separate electrode(s) or electrode pairs are used for pacing the RA 8. Similarly, In accordance with a preferred embodiment of the present invention, The lead 4 may include more than one electrode or pair of electrodes (not shown) which may be separately used for sensing and for pacing the right ventricle 9. Yet similarly, the lead 6 may include more than one electrode or electrode pairs (not shown) of which one or more electrode or electrode pair is used for sensing in the left ventricle 10 and one or more additional electrodes or electrode pairs are used for delivering non-excitatory ETC signals to the left ventricle 10.

It will therefore be appreciated by those skilled in the art, that the number and arrangement of the electrodes within the leads 2,4 and 6 may be varied in many ways and many combinations all being within the scope and spirit of the present invention.

Various types of electrodes and electrode positioning methods known in the art may be used for sensing and pacing and for delivering ETC signals to

the heart. One or more of the electrodes or electrode pairs 2A, 4A and 6A may be implanted within a cardiac chamber and placed in contact with the endocardium as disclosed hereinabove. One or more of the electrodes or electrode pairs 2A, 4A and 6A may also be disposed within a cardiac blood vessel, such as a lateral vein of the GCV or another suitable cardiac blood vessel, and used for sensing and/or pacing and/or delivering ETC signals to the myocardial tissue adjacent to or in contact with the blood vessel wall. One or more of the electrodes or electrode pairs 2A, 4A and 6A may also be epicardial electrodes which may be epicardially applied to the heart as is well known in the art.

Typically, ETC signals are delivered to the left ventricle via the electrode(s) 6A of lead 6. The timing of the ETC signal is triggered by locally sensing in the LV the depolarization wave of the PE or the SE. Preferably, a separate sensing electrode (not shown) which is also included within the lead 6 and is positioned in the vicinity of the electrode(s) 6A, is used for the local sensing in or about the LV 10, since the type and surface area optimal for sensing electrodes are usually different than the type and surface area of electrodes which are optimized for delivering the relatively large currents of ETC signals. However, it may also be possible to use the same electrode (or electrodes) 6A for delivering the ETC signal and for locally sensing the depolarization wave in or about the LV 10.

To facilitate correct timing of the ETC delivery, measures need to be taken so that ETC signal delivery is not triggered by local LV sensing of noise, premature ventricular contractions (PVCs), premature atrial contractions (PACs) or by delayed sensing of remote events such as a right ventricular depolarization. One possible approach is the restricting of the local sense triggering for ETC delivery to a predefined time window.

The use of a predefined time window for other different purposes such as to detect activation for capture verification in pacemakers is known in the art. U.S. Patent 5,443,485 to Housworth et al. discloses the use of a timing window to detect a paced stimulation pulse for achieving capture verification to ensure that the pacing pulse energy is high enough.

U.S. Patent 5,683,431 to Wang discloses a method for performing pacemaker capture verification using electrodes different than the pacing electrodes to sense the activation evoked by the pacing pulse.

U.S. Patent 5,391,192 to Lu et al. discloses a method for externally determining the minimum energy of a pacing pulse for capture verification using window based detection of activation.

Reference is now made to Fig. 2 which is a schematic diagram useful in understanding a method using an alert window for timing the delivery of ETC signals useful in operating the device of Fig. 1, in accordance with a preferred embodiment of the present invention. The detection time window is referred to as the "alert window" throughout the present application.

The horizontal axis of Fig. 2 represents time. The arrow labelled 11 schematically represents the timing of a depolarization event 11 locally sensed in the RV by one or more electrodes (not shown) of the lead 4 of Fig. 1. The time $T_0$ represents the time of detection of the RV event. Typically, the time $T_0$ represents the time point at which a threshold crossing occurs. However, $T_0$ may also represent the time of event detection obtained by other methods known in the art for cardiac event detection such as detection methods based on the shape of the signal (also known as signal morphology based detection methods) or other suitable detection methods known in the art. The RV event 11 may represent a locally sensed RV depolarization initiated by a naturally occurring SA node evoked atrial event (not shown) or initiated by artificial atrial pacing. The RV event 11 may also represent a locally sensed RV depolarization initiated by a pacing pulse delivered to the RV through an electrode (not shown) included in the lead 4 of Fig. 1. After the time $T_0$, a local sense "refractory" period labeled $\Delta T1$ begins. The refractory period $\Delta T1$ ends at time $T_R$. During the refractory period $\Delta T1$ no sensing is performed. This refractory period is used to avoid the electrical pacing artifact due to electrode polarization and/or electrode cross-talk. The refractory period may also be useful in avoiding electrical artifacts due to far field sensing as is well known in the art.

Typically, the duration of the refractory period $\Delta T1$ is approximately 10 -15 milliseconds but other values may be used depending, *inter alia*, on the specific application, electrode type, and detection method used. It is noted that, in accordance with one preferred embodiment of the present invention, the value of the refractory period duration may be set to $\Delta T1=0$. In such an embodiment no refractory period $\Delta T1$ is implemented.

A local sense alert window having a duration $\Delta T3$ starts at time $T_1$ and ends at time $T_3$. The time interval between time points $T_0$ and $T_1$ is defined as the alert window delay interval $\Delta T2$ which is the delay between time of detection of the depolarization event 11 and the beginning of the alert window $\Delta T3$.

The arrow labeled 12 of Fig. 2 schematically represents the occurrence of a depolarization event locally sensed in the LV. For example, the locally sensed event 12 may be sensed by a sensing electrode (not shown) or by an ETC signal delivery electrode (not shown) included within the lead 6 of Fig. 1. The time $T_2$ represents the time of detection of the LV depolarization event 12. Typically, the time $T_2$ represents the time point at which a threshold crossing occurs as is disclosed hereinbelow. However, $T_2$ may also represent the time of event detection obtained by other methods known in the art for cardiac event detection.

An article titled "NEURAL NETWORK BASED ADAPTIVE MATCHED FILTERING FOR QRS DETECTION" by Xue et al., published in IEEE Transactions on Biomedical engineering, Vol. 39, No. 4 pp. 317-329 (1992) and incorporated herein by reference, discloses an adaptive matched filtering algorithm based on an artificial neural network for QRS detection.

An article titled "IDENTIFICATION OF VENTRICULAR TACHYCARDIA WITH USE OF THE MORPHOLOGY OF THE ENDOCARDIAL ELECTROGRAM" by Langberg et al., published in Circulation, Vol. 77, No. 6 pp. 1363- 1369 (1988) and incorporated herein by reference, discloses the application of a template to derive morphological parameters of unipolar and bipolar electrogram signals for detecting tachycardia.

An article titled "CLASSIFICATION OF CARDIAC ARRHYTHMIAS USING FUZZY ARTMAP" by F.M. Ham and S. Han, published in IEEE

Transactions on Biomedical engineering, Vol. 43, No. 4 pp. 425-430 (1996) and incorporated herein by reference, discloses the use of a fuzzy adaptive resonance theory mapping (ARTMAP) neural net classifier for classifying QRS complexes under normal and abnormal conditions.

U.S. Patent 5,782,876 to Flammang titled "METHOD AND APPARATUS USING WINDOWS AND AN INDEX VALUE FOR IDENTIFYING CARDIAC ARRHYTHMIAS", incorporated herein by reference, discloses the use of the sensed electrogram slope (derivative of ECG) for morphological electrogram detection in a device for identifying cardiac arrhythmias.

The above referenced morphological signal detection methods, as well as other signal morphology based detection methods known in the art, may be adapted for detection of the depolarization events within the IEGM signals of the present invention.

The detection of the LV sensed event 12 at time $T_2$ triggers the delivery of an ETC signal represented by the cross hatched area labeled ETC. The ETC signal starts at a time point $T_4$ separated from $T_2$ by a delay interval $\Delta T4$. The ETC signal has a duration $\Delta T5$.

Preferably, the value of the duration of the ETC signal $\Delta T5$ is a variable duration and may vary from one beat cycle to another in accordance with the required modification of myocardial contractility. Typically, the duration and or other parameters of the ETC signal may be modified based on the current value of the heart rate. The methods for determining the required ETC signal duration $\Delta T5$ are not the subject matter of the present invention and will not be disclosed in detail hereinafter.

It is noted that, in accordance with other preferred embodiments of the present invention, the duration of the ETC signal $\Delta T5$ may be a constant value which does not vary from one beat cycle to another beat cycle.

The ETC signals may have various waveforms, durations and intensities as disclosed in detail by Ben Haim et al. in the above referenced International Publications No. WO 97/25098, WO 98/10828, WO 98/10829, WO 98/10830, WO 98/10831 and WO 98/10832. The characteristics of the delivered ETC

signals are not the subject of the present invention and will not be further discussed hereinafter.

Only a locally sensed depolarization event detection occurring within the duration of the alert window $\Delta T3$ is used to trigger an ETC signal. The detection of an electrical depolarization event happening outside the alert window will not result in triggering of an ETC signal. This has the advantage of reducing the probability of delivering an improperly timed ETC signal due to electrical noise occurring outside the preset duration of the alert window $\Delta T3$. However, if a depolarization event (not shown) due to an ectopic beat is detected between the time $T_0$ and the time $T_1$ in a case where the refractory period $\Delta T1$ is not used, or between the time $T_R$ and the time $T_1$ in a case where the refractory period $\Delta T1$ is used, and then a later depolarization event (not shown) is detected within the duration of the alert window $\Delta T3$, the triggering of an ETC signal by the later occurring depolarization event may result in an improperly timed ETC signal. Therefore, In order to prevent such improper timing, the timing method may further include an inhibitory window $\Delta TI$. Any depolarization event which is detected within the duration of the inhibition window $\Delta TI$ will result in the inhibiting of ETC signal delivery within the current beat cycle as disclosed in detail hereinbelow.

In accordance with one preferred embodiment of the present invention, $\Delta TI = \Delta T2 - \Delta T1$, in such a preferred embodiment the inhibition window $\Delta TI$ starts at the end of the refractory period $\Delta T1$ and ends at the beginning of the alert window $\Delta T3$. If no refractory period is used ($\Delta T1=0$), the inhibition window spans the entire alert window delay interval $\Delta T2$. However, in accordance with other preferred embodiments of the timing method of present invention, the end of the inhibition period $\Delta TI$ may be separated from the beginning of the alert window $\Delta T3$ by an intermediate time interval (not shown in Fig. 2 for the sake of clarity of illustration). The detection of a depolarization event within the duration of such an intermediate time interval will not result in the inhibition of triggering of an ETC signal by a later depolarization event detected within the duration of the alert window $\Delta T3$.

If a depolarization event was detected in the IEGM signal which is locally sensed in the left ventricle 10 within the duration of the inhibition window ΔTI, ETC signal delivery is inhibited such that later occurrence of a depolarization event within a preset "inhibition refractory period" (not shown in Fig. 2 for the sake of clarity of illustration) of the current beat cycle will not result in a delivery of an ETC signal. This feature has the advantage that it reduces the probability of erroneous detection of spurious noise or of ectopic beats such as PVCs or PACs and the subsequent triggering of the delivery of an incorrectly timed ETC signal. The details of the implementation of the inhibition refractory period are disclosed in detail in International Application No. PCT/IL00/00126 Titled "APPARATUS AND METHOD FOR TIMING THE DELIVERY OF NON-EXCITATORY ETC SIGNALS TO A HEART".

Typically, the local sensing sensitivity is adjusted such that, only events of a certain amplitude will be detected. This is achieved by setting a detection threshold. Threshold crossing detection methods for electrical signals are well known in the art and are not the subject matter of the present invention. Such threshold crossing detection methods are commonly used in pacemakers for sensed event detection.

Briefly, any acceptable detection method based on threshold crossing of one or more threshold levels may be used with the present invention. For example, the sensed electrogram may be biphasic, and two threshold levels may be used including a positive threshold level and a negative threshold level. Alternatively, full wave rectification of the electrogram may be used to obtain a signal which is positive only, such that a single positive threshold level may be used. Additionally, other methods of detection may be used which are based on signal morphology as disclosed in detail hereinabove.

Since multiple threshold crossings may occur during the same depolarization event or during noise signals, ambiguity may arise as to which threshold crossing should be used as the trigger. This may be solved by triggering by the first threshold crossing in the window and by implementing an "alert refractory period" ΔT7 following the first threshold crossing of the LV sensed event 12 at time $T_2$ to prevent multiple triggering by multiple threshold

crossings occurring within a single depolarization wave representing a single event. The alert refractory period $\Delta T7$ starts at the time $T_2$ and has a fixed duration represented by the double headed arrow labeled $\Delta T7$. During the alert refractory period $\Delta T7$ no sensing is performed so that additional triggering cannot happen during the period $\Delta T7$.

It is noted that, since the first threshold crossing due to an LV sensed event 12 may happen at any time during the alert window $\Delta T3$, and since the duration of the ETC signal $\Delta T5$ may be varied from one beat cycle to another (for varying the effects of the ETC signal on myocardial contraction), the duration of the alert refractory period $\Delta T7$ is set such that it is larger than the sum of the durations of the alert window $\Delta T3$, the delay interval $\Delta T4$ and the maximal allowable duration $\Delta T5_{MAX}$ of the ETC signal. The maximal allowable duration $\Delta T5_{MAX}$ is a preset value.

Thus, $\Delta T7 > \Delta T3 + \Delta T4 + \Delta T5_{MAX}$ . This ensures that no further threshold crossings will be sensed and detected after the first threshold crossing detection until the ETC signal has ended, irrespective of the time of occurrence of the first threshold crossing detection $T_2$ within the alert window duration $\Delta T3$ and of the specific duration $\Delta T5$ of the ETC signal delivered within the current beat cycle.

Typically, the duration $\Delta T3$ of the alert window is approximately 30 milliseconds, the duration of the delay interval $\Delta T4$ is approximately 60 milliseconds and the maximal allowable duration $\Delta T5_{MAX}$ of the ETC signal is approximately 20-30 milliseconds. However, other values of $\Delta T3$ , $\Delta T4$ and $\Delta T5_{MAX}$ may be used.

A typical value of the duration of the alert refractory period $\Delta T7$ is therefore approximately 150-200 milliseconds. However, other values of the duration of the alert refractory period $\Delta T7$ may be used depending, *inter alia*, on the particular values of $\Delta T3$ , $\Delta T4$ and $\Delta T5_{MAX}$ used. The duration of the alert refractory period $\Delta T7$ is a preset value and does not change from one beat cycle to another. However, the duration of the alert refractory period $\Delta T7$ may be changed if necessary by appropriately reprogramming the software

embedded within the device 1 telemetrically or non-telemetrically (depending on the specific hardware implementation of the device 1).

For the sake of simplicity of presentation, the method of the present invention will be disclosed as using a single positive threshold level. A certain positive threshold voltage level is set for the pacemaker/ETC device. A crossing of this threshold level by the IEGM signal occurring within the time interval between $T_R$ and $T_3$ will be detected as an event. For example, the detection threshold may be set as +3.0 millivolts but other suitable threshold levels may also be used for detection, depending, *inter alia*, on the placement and quality of contact of the sensing electrode or electrodes with the cardiac site at which the sensing is performed. A refractory period of approximately 150 - 200 milliseconds starting at the time of detection of threshold crossing, may be used to prevent multiple threshold crossing detections, but other suitable values of the sense refractory period may also be used. In accordance with one preferred embodiment of the present invention, the use of the refractory period may be implemented as disclosed in detail in the above referenced International Application No. PCT/IL00/00126 Titled "APPARATUS AND METHOD FOR TIMING THE DELIVERY OF NON-EXCITATORY ETC SIGNALS TO A HEART".

In accordance with another preferred embodiment of the present invention, the ETC device or pacemaker/ETC device of the present invention may continuously perform morphological analysis on the IEGM signal locally sensed in or about the left ventricle (or at a cardiac site in the vicinity of the cardiac site at which the ETC signal is to be delivered) for the entire duration of the alert window period, and the decision as to which of the depolarization events (provided that there was more than one such depolarization event within the alert window duration) is to be used as the ETC signal triggering event may be made based on the results of the morphological analysis which determine the depolarization event which gives the best match according with predetermined morphological criteria. After determining the event which is to be used as the ETC signal trigger, the timing of the delivery of the ETC signal is determined as disclosed in detail in International Application No.

PCT/IL00/00126 Titled "APPARATUS AND METHOD FOR TIMING THE DELIVERY OF NON-EXCITATORY ETC SIGNALS TO A HEART", cited hereinabove.

It will be appreciated that any suitable method of morphological analysis known in the art including but not limited to the methods disclosed by Xue et al., Langberg et al., Ham and Han, and Flammang, may be used for morphological analysis in the method of the present invention, provided that the processor or controller used in the ETC device or pacmaker/ ETC device has sufficient processing power.

It is noted that, many other suitable methods of event detection, including but not limited to the methods of using IEGM single threshold crossing, IEGM multiple threshold crossings, IEGM derivative (for signal slope determination), signal morphology detection methods or combinations thereof may be used in the ETC signal timing method of the present invention.

The conduction characteristics of the myocardium of a patient may vary considerably. Among the factors influencing the conduction velocity of the myocardium are electro-physiological changes induced in the myocardium due to patient exercise, increased metabolic activity or stress. These changes may be mediated, *inter alia*, by noradrenaline and other hormones which are released into the circulation and affect the myocardial conduction velocity or by sympathetic (or parasympathetic in some cases) neural control of cardiac tissue. Such mechanisms may lead to changes in the heart rate through their effects on the natural SA node pacemaker. Thus, under conditions of patient exercise, increased metabolic activity or stress, the heart rate increases and the conduction velocity of the myocardial depolarization wave increases. This increase in conduction velocity causes the electrogram signal sensed in the LV by the lead 6 (Fig. 1) to be shifted in time such that the time interval $T_2 - T_0$ decreases and may be smaller than $T_1$ which results in the locally sensed event 12 falling outside of the alert window and within the inhibition window $\Delta TI$, which will lead to active inhibition of the delivery of the ETC signal. Slowing of the heart rate may cause the IEGM signal sensed in the LV by the lead 6 (Fig. 1) to be shifted in time such that the time $T_2$ of occurrence of the locally sensed event

12 occurs later within the alert window ΔT3 of Fig. 2, or occurs at a time point later than the time point $T_3$, which is outside of the alert window ΔT3 ,in which case no triggering will occur.

Additionally, the conduction velocity of a paced event in the myocardium is slower than the conduction velocity of the depolarization wave evoked by a naturally evoked sinus rhythm.

Another factor influencing the myocardial conduction velocity is the delivery of ETC signals to the myocardium. During the application of ETC signals to the myocardium the conduction velocity of myocardial depolarization may be modified. The conduction velocity may be increased or decreased depending, *inter alia*, on the type of ETC signal which is delivered to the myocardium.

Thus, the conduction velocity and consequently the time interval between the RV sensed event and the LV sensed event are heart rate dependent and may depend on other cardiac conditions.

In accordance with one embodiment of the present invention, the method of timing of the delivery of the ETC signal uses a fixed alert window delay period (ΔT2) and a fixed alert window duration (ΔT3) which is wide enough to enable acceptably accurate detection under a variety of conditions involving different myocardial conduction velocity values. A single set of alert window parameters is determined which includes the detection threshold value used for triggering within the alert window, the alert window starting time point $T_1$ and the alert window end time point $T_3$. This alert window parameter set is determined such as to enable an acceptable level of detection of events for all or most of the conditions involving different myocardial conduction velocity values . The pacemaker/ETC device 1 may then be programmed with this determined single set of alert window parameters as is disclosed in detail hereinafter. In this preferred embodiment of the present invention, once the alert window parameters are determined, the implanted pacemaker/ETC device 1 is programmed with these parameters and uses the same set of alert window parameters for the timing of the delivery of the ETC signals as disclosed hereinabove. The above referenced International Application No.

PCT/IL00/00126 Titled "APPARATUS AND METHOD FOR TIMING THE DELIVERY OF NON-EXCITATORY ETC SIGNALS TO A HEART", discloses a method and apparatus for timing the delivery of ETC signals to a heart using an alert window having preset fixed parameters.

However, it may be advantageous to use a plurality of different sets of alert window parameters. The use of a plurality of different alert window parameters is desirable since excessive widening of the alert window duration which may be required for suitable event detection under a variety of different patient cardiac conditions when a single alert window parameter set is used, may result in an increased probability of spurious detection of noise and/or ectopic events. In contrast, when a plurality of alert window parameter sets are used, the delay and duration of each specific alert window may be better adapted to a particular patient condition, such as but not limited to a particular heart rate, by modifying the alert window parameters sufficiently to position the alert window at the time period most proper for event detection to acceptably reduce the probability of detection of spurious noise and/or ectopic events.

Each set of alert window parameters includes data which may be used to calculate in real time the values of $T_1$ and $T_3$ which are optimized for a specific condition or for a specific range of conditions. The data of each set are determined so as to optimize detection of LV locally sensed events under the specific condition without unduly increasing spurious triggering. This method may be of particular advantage in patients in which the myocardial conduction velocity substantially varies between the different conditions disclosed hereinabove and in which the use of a single set of alert window parameters may lead to significant inaccuracies in the detection of the locally sensed event or in the timing of the ETC signal delivery during at least one of the various different conditions leading to changes of myocardial conduction velocity disclosed hereinabove. Such inaccuracies may occur due to a shift of the time of occurrence of the LV locally sensed event which may increase the probability of such a sensed event occurring out of the alert window time interval. This will cause a certain percentage of the LV locally sensed events to go undetected, so that not every LV locally sensed event will trigger the delivery of an ETC signal.

While this may not by itself endanger the patient, it may lead to a reduction in the desired effect of the ETC signal on cardiac contractility. However, the use of a single common set of window parameters under varying conditions may result in increased rate of incorrect triggering of ETC signal delivery by spurious noise or by PVCs. This may lead to delivery of ETC signals outside of the inexcitable myocardial period which may be arrhythmogenic.

Therefore, in accordance with another preferred embodiment of the present invention, the implanted device 1 is programmed with a plurality of predetermined alert window parameter sets. Each of the predetermined parameter sets includes data for computing the values of $T_1$ and $T_3$ of the alert window in real time and may also include a detection threshold value. If a detection method using morphological IEGM parameters is used the alert window parameter sets may also include morphological parameter data useful for detecting a depolarization event. Each set of alert window parameters is optimized for use under specific conditions. For example, different alert window parameter sets may be used for different ranges of heart rates as is disclosed in detail hereinafter. Other different sets of alert window parameters may be used for paced events, sensed events, and for events occurring in periods during which ETC signals are delivered to the myocardium.

Systems and methods for determining alert window parameters

The present invention discloses, *inter alia*, systems and methods for determination of the alert window parameters.

Reference is now made to Fig. 3A which is a schematic diagram illustrating a system for determining and programming alert window parameters for an implanted ETC device or pacemaker/ETC device, in accordance with a preferred embodiment of the present invention. The system 20 includes an implanted ETC device 19 and an analyzing unit 23. The implanted ETC device 19 further includes electronic circuitry (not shown in Fig. 3A for the sake of clarity of illustration) for event sensing and for delivering ETC signals, the details of such circuitry are disclosed in detail hereinafter. The implanted ETC device 19 may or may not include pacing circuitry (not shown in Fig. 3A for the sake of

clarity of illustration) for pacing the heart as is disclosed in detail hereinafter. The implanted ETC device 19 is suitably connected to one or more implantable leads 22 and includes a telemetry unit 26 for wirelessly communicating with the analyzing unit 23. The analyzing unit 23 includes a telemetry unit 28 for wirelessly communicating with the telemetry unit 26 of the pacemaker/ETC device 19. The analyzing unit 23 further includes a processing unit 30 in communication with the telemetry unit 28 for receiving data from the telemetry unit 28 and for storing and processing the received data. The analyzing unit 23 further includes a display unit 32 suitably connected to the processing unit 30 for displaying graphic symbolic and numerical data processed by the processing unit 30. The processing unit 30 may be a computer, a personal computer, a workstation, a mainframe or any other type of computing device capable of storing and processing data. The display unit 32 may be a cathode ray tube (CRT) display, a video monitor, an LCD display or any other suitable type of display or monitor. The analyzing unit 23 further includes one or more user interfaces 31 for enabling a user such as a cardiologist or another operator to control the operation of the analyzing unit 23. The user interface 31 may be a keyboard, a pointing device or any other suitable user interface device or a combination of user interface devices which are known in the art.

Reference is now made to Fig. 3B which is schematic functional block diagram illustrating the details of an implantable device for pacing the heart, for delivering ETC signals to the heart and for data acquisition and processing usable as the implantable device of the system of Fig. 3A, in accordance with a preferred embodiment of the present invention. The implantable pacemaker/ETC device 21 is a preferred version of the implantable device 19 of Fig. 3A suitable for use within the system 20 of Fig. 3A The pacemaker/ETC device 21 includes a pacing core 34 for providing pacing pulses to the RA and RV pacing electrodes (not shown) of the implantable leads 22. The pacemaker/ETC device 21 further includes sense amplifier units 36 for amplifying the RA, RV and LV signals locally sensed by the sensing electrodes (not shown) of the implantable leads 22. For example, when the pacemaker/ETC device 21 represents the pacemaker/ETC device 1 of Fig. 1,

one of the sense amplifier units 36 receives the signal locally sensed in the RA 8 from lead 2 of Fig. 1, another of the sense amplifier units 36 receives the signal locally sensed in the RV 9 from lead 4 of Fig. 1 and a third one of the sense amplifier units 36 receives the signal locally sensed in the LV 10 from the lead 6 of Fig. 1.

The pacemaker/ETC device 21 further includes sensing units 38 suitably connected to a controller unit 40. The sensing units 38 receive the amplified locally sensed signals from the amplifier units 36 and provide trigger signals to the controller unit 40 for activating the pacing core as is known in the art. The pacemaker/ETC device 21 further includes timing units 42, connected to the controller unit 40 for providing the controller unit 40 with clock signals, and a memory unit 44 suitably connected to the controller unit 40. The controller 40 can store data in the memory unit 44 and can access the data stored in the memory unit 44 for processing the accessed data and/or for sending data to a telemetry unit 26 for telemetrically communicating the data to a receiving station (not shown) placed outside of the patient. The memory unit 44 may include random access memory (RAM) units (not shown), read only memory (ROM) units (not shown), other suitable type of memory units known in the art, or any suitable combination of memory unit types.

It is noted that the pacemaker/ETC device 21 when connected to implantable leads having the configuration of leads 2, 4, and 6 of Fig. 1, may function, *inter alia*, as a pacemaker in a DDD mode, which includes, *inter alia*, the ability to detect PVCs by using PVC detection methods known in the art. For example, PVC detection may be performed by the circuitry of the pacemaker/ETC device 21 using dual chamber event sequence analysis methods as is known in the art. However, other methods known in the art for PVC detection may also be used.

The telemetry unit 26 is used for wirelessly transmitting data stored in memory unit 44 under the control of the controller unit 40. The pacemaker/ETC device 21 further includes an excitable tissue controller (ETC) unit 50. The ETC unit 50 is suitably connected to the controller unit 40 and to one or more ETC electrodes (not shown) within the leads 22. For example, when the

pacemaker/ETC device 21 represents the pacemaker/ETC device 1 of Fig. 1, the ETC unit 50 is connected to the ETC signal delivering electrode 6A of the lead 6 of Fig. 1 . However in other preferred embodiments of the present invention, the ETC unit 50 may be connected to one or more ETC electrodes or ETC electrode pairs (not shown) which are used for delivering ETC signals. The controller unit 40 controls the delivery of ETC signals to the myocardium by timing the delivery of suitable control signals to the ETC unit 50.

Reference is now made to Fig. 4 which is schematic functional block diagram illustrating the details of another implantable device for delivering ETC signals to the heart and for data acquisition and processing which is usable as the implantable device of the system of Fig. 3A, in accordance with another preferred embodiment of the present invention. The device 24 is similar to the device 21 of Fig. 3A except that it does not include the pacing core 34 of the device 21 of Fig. 3A and is not capable of pacing.

The device 24 may be used in patients where ETC signals need to be delivered to the heart for modulating cardiac contractility but pacing of the heart is not required, such as but not limited to congestive heart failure (CHF) patients. CHF patients may have an unimpaired cardiac conduction system and may exhibit no chronotropic incompetence. In the cases where the device 24 is used for delivering ETC signals to the heart, the electrodes (not shown) in the implantable leads 22 are used for sensing and for delivering ETC signals and are not used for pacing the heart.

In operation, the data stored in the memory unit 44 of the devices 21 and 24 of Figs. 3A and 4, respectively, is telemetrically transmitted by the telemetry unit 48 to the analyzing unit 23 (Fig. 3A) which is disposed outside the patient for processing, storage and display. The system 20 of Fig. 3A may graphically display the data on the display unit 32. The displayed data is used by the user or physician to determine the alert window parameters as is disclosed in detail hereinafter. Alternatively, the alert window parameters may be automatically determined and displayed for approval by the user or the physician.

In accordance with another preferred embodiment of the present invention, the alert window parameters may be determined by non-telemetrically

communicating the locally sensed IEGM signals sensed in a patients heart to a processing and analyzing system disposed outside the patient.

Reference is now made to Fig. 5 which is a schematic diagram illustrating a system 60 for pacing the heart, for delivering non-excitatory ETC signals and for non-telemetrically determining and programming alert window parameters for an ETC device or pacemaker/ETC device, in accordance with another preferred embodiment of the present invention. The system 60 includes a plurality of implantable leads 22 implanted within a patient (the patient is not shown) and an analyzing unit 64. The plurality of implantable leads 22 may include, for example, the leads 2, 4 and 6 of Fig. 1. However, the plurality of leads 22 may include any other suitable combinations of leads including a plurality of sensing, pacing and ETC electrodes positioned in two or more chambers of the heart as disclosed for the devices 1 , 19, 21 and 24 hereinabove.

The plurality of leads 22 are implanted in the patient's heart and are then suitably connected to the analyzing unit 64 for data acquisition to collect data for determining the alert window parameters.

The analyzing unit 64 includes a processing unit 61, a front-end unit 62, an analog to digital converting unit (A/D) 63, a pacing unit 68 and an ETC unit 65. The front end unit 62 is suitably connected to one or more of the sensing electrodes of the leads 22 and to the processing unit 61 for pre-conditioning one or more IEGM signals sensed by these one or more sensing electrode. The front–end unit 62 may include suitable circuitry such as one or more amplifier circuits (not shown) for amplifying the IEGM signals sensed by the one or more sensing electrodes. The front-end unit 62 may also include filter circuits (not shown) for filtering the amplified signals prior to digitizing them by the A/D unit 63. The front-end unit 62 is suitably connected to the A/D unit 63 and provides amplified or amplified and filtered IEGM signals thereto for digitizing.

The A/D unit 63 may include one or more separate A/D converters (not shown) each A/D converter being dedicated to a single sensing electrode of the one or more sensing electrodes. Alternatively, the A/D unit 63 may include a single A/D converter (not shown) suitably connected to a plurality of sensing electrodes of the leads 22 through a multiplexer unit (not shown). The digitized

IEGM signals are provided to the processing unit 61 by the A/D unit 63 for further processing. The processing unit 61 digitally performs the detection of events based on the digitized IEGM data provided by the A/D unit 63. The analyzing unit 64 further includes a memory unit 66 suitably connected to the processing unit 61 for storing data.

The pacing unit 68 is suitably connected to the processing unit 61 and to one or more pacing electrodes of the leads 22. The pacing unit 68 receives control signals from the processing unit 61 for controlling the delivery of pacing pulses to one or more locations in the heart (not shown). The pacing unit 68 includes all the necessary circuitry for delivering pacing pulses to one or more pacing electrodes. Such circuitry is well known in the art and is not shown in detail hereinafter.

It is noted that the analyzing unit 64 when connected to the implantable leads 22 is capable of performing all the functions of an implanted pacemaker. For example, when the leads 22 have the configuration of leads 2, 4, and 6 of Fig. 1, the analyzing unit 64 is capable of performing, *inter alia*, all the functions of an implanted pacemaker in a DDD mode. These functions include, *inter alia*, the ability of detection of PVCs as is well known in the art.

The ETC unit 65 is suitably connected to the processing unit 61 and to one or more ETC signal delivery electrodes of the implantable leads 22. The ETC unit 65 receives control signals from the processing unit 61 for controlling the delivery of ETC signals to the heart through the one or more ETC delivery electrodes of the implantable leads 22.

The ETC unit 65 may be any suitable unit for delivering ETC signals having various waveforms, durations and intensities as disclosed in detail by Ben Haim et al. in the above referenced International Publications No. WO 97/25098, WO 98/10828, WO 98/10829, WO 98/10830, WO 98/10831 and WO 98/10832. The characteristics of the delivered ETC signals are not the subject of the present invention and will not be further discussed hereinafter.

The system 60 further includes a display unit 32 suitably connected to the processing unit 61 for displaying graphic symbolic and numerical data processed by the processing unit 61 as disclosed hereinabove for the analyzing

system 20 of Fig. 3A. The system 60 may further include a data storage unit 67 for storing data. The data storage unit 67 may be any suitable data storage device for storing data on a storage medium such as a magnetic storage medium, an opto-magnetic storage medium, an optical storage medium, a holographic storage medium or any other type of fixed or removable storage medium. Some non-limiting examples of the storage device are, a magnetic hard disk drive, a magnetic floppy disk drive, an opto-magnetic disk drive, an optical disc drive. The data stored on the data storage device may include, *inter alia*, patient clinical data, patient demographic data, various IEGM and histogram data collected in the process of determining the alert window parameters and various determined alert window parameter sets. The data storage device may be used for storing data for a plurality of different patients.

The system 60 further includes one or more one user interface devices 69 suitably connected to the processing unit 61 through a suitable communication interface (not shown) for enabling the user of the system 60 to input data and commands for controlling the operation of the analyzing unit 64. The user interface device(s) 69 may be a keyboard, a pointing device such as a mouse, a light pen in combination with a suitable touch sensitive screen or tablet, or any other suitable device for inputting data or commands to the analyzing unit 64, or any suitable combination thereof.

In operation, after the leads 22 are implanted in the heart of the patients and are connected to the analyzing unit 64, the analyzing unit 64 is operated to collect data for determining the parameter sets for the alert window under various conditions as is disclosed in detail hereinafter. It is noted that the analyzing unit 64 is capable of performing all the activities of an implanted pacemaker/ETC device such as the pacemaker/ETC device 21 of Fig. 3A except for the telemetry functions. The analyzing unit 64 may perform cardiac pacing at one or more cardiac locations and may controllably deliver ETC signals to one or more cardiac locations. The performance of the functions of a pacemaker/ETC device by the analyzing unit 64 may be achieved by using different methods and/or different hardware implementation than the methods and hardware of an implantable pacemaker/ETC device. For example, while in

the pacemaker/ETC device 21 the event detection is performed by sensing units 38 which are analog circuits, the event detection in the analyzing unit 64 is performed by digitally processing the digitized IEGM data provided by the A/D unit 63. Additionally, the pacing unit 68 and the ETC unit 65 may have hardware and software implementations different than those of the pacing core 34 and the ETC unit 50, respectively, of the pacemaker/ETC device 21 because of the physical size and current consumption limitations imposed on the design of the pacing core 34 and the ETC unit 50 of the pacemaker/ETC device 21. These limitation are not relevant in the non-implanted analyzing unit 64. However, functionally, the sensing, pacing and ETC delivery of the analyzing unit 64 are similar to and may be regarded as simulating the same functions of an implanted of the pacemaker/ETC device, such as, for example, the functions of the pacemaker/ETC device 21 of Fig. 3A. Therefore, after the different alert window parameter sets are determined using the analyzing unit 64, these alert window parameter sets may be used to program an implanted pacemaker/ETC device and are used to operate the programmed implanted pacer/ETC device after it has been suitably connected to the implantable leads 22 and implanted in the patient.

Reference is now made to Fig. 6 which is a schematic functional block diagram illustrating a system 70 for delivering non-excitatory ETC signals and for non-telemetrically determining alert window parameters for use in an ETC device, in accordance with another preferred embodiment of the present invention.

The system 70 includes an external non-implanted analyzing unit 74 suitably connected to a plurality of implantable leads 22. The analyzing unit 74 of Fig. 6 is similar to the analyzing unit 64 of Fig. 5, except that it does not include the pacing unit 68. The analyzing unit 74 operates similarly to the analyzing unit 64, except that it does not have the pacing capacity of the analyzing unit 64 and is therefore not capable of pacing of the heart.

It is noted that, while the devices 1, 19, 21 and 24 of Figs. 1,3, 3A and 4 ,respectively, and the systems 60 and 70 of Figs. 5 and 5A, respectively, may use the single threshold crossing detection method disclosed in detail

hereinabove, all of these devices and systems may use other detection methods. The detection methods for detecting depolarization events in the IEGM signals sensed by one or more of the electrodes or electrode pairs included in one or more of the implantable leads such as the leads 2,4, and 6 of the device 1 and the plurality of implantable leads 22 of the devices 19, 21 and 24 and the systems 60 and 70, may include any suitable detection methods known in the art for detection of locally sensed cardiac depolarization events based on signal morphology and/or methods based on multiple threshold crossings and/ or signal slope or any combinations thereof as disclosed hereinabove.

Typically, the data acquisition method of the present invention includes automatically varying the detection threshold levels and cumulatively recording data of threshold crossing events at predefined time bins starting at the time of detection of an RV event ($T_0$ of Fig. 2).

After implantation of the pacemaker/ETC device 21 the pacing parameters are set (including, *inter alia*, the pacing voltage, the pacing pulse width, and other relevant pacing parameters.), data acquisition and processing will take place as explained hereinbelow. If the device 24 or the system 70 are used for data acquisition no pacing parameters need be set since the device 24 and the system 70 have no pacing capability and no pacing is performed thereby.

It is noted that in accordance with a preferred embodiment of the present invention data acquisition may also be performed by implanting the implantable electrodes 22 in a patient and then operatively connecting the implantable leads 22 to the external analyzing unit 64 of the system 60 of Fig. 5 or to the external analyzing unit 74 of the system 70 of Fig. 6. The pacing parameters of The external analyzing unit 64 of the system 60 are set (including, *inter alia*, the pacing voltage, the pacing pulse width, and other relevant pacing parameters), and data collection may be then performed while the patient is recovering from the electrode implantation procedure for as long as the electrodes 22 implanted in the patient are connected to the analyzing unit 64. Similarly data may be collected by operatively connecting the implanted electrodes 22 to the analyzing unit 74 wherein no pacing is performed.

While the data collected from a patient with an implanted device may be different from data collected from a hospitalized patient using the systems 60 and 70, the cardiac conditions of the patient may be altered by instructing the patient to perform certain types of physical activity while he is in bed.

For the sake of simplicity, the following description of the data acquisition method relates to freely moving patients having an implanted pacemaker/ ETC device such as the device 21 of Fig. 3A. However, it will be appreciated that the methods are also adaptable to patients in which the device 24 or one of the systems 60 and 70 is used, by suitably adapting and modifying the methods to the different patient conditions or to the absence of cardiac pacing when the device 24 or the system 70 are used.

Data acquisition

After implantation of the pacemaker/ETC device 21 in the patient, the patient is sent home for a time period which is estimated as sufficient for collecting enough data such as a few days or weeks. The patient is instructed to carry out daily routine behavior. The pacemaker/ETC device 21 records data as is disclosed in detail hereinafter. The data is then offloaded from the pacemaker/ETC device 21 telemetrically as disclosed hereinabove. The off-loaded data is then stored for further processing by the analyzing unit 23 of Fig. 3A.

Record data structure

Reference is now made to Fig. 7 which is a schematic diagram illustrating the structure of a typical data collection time interval useful in the acquisition of data histograms, in accordance with a preferred embodiment of the present invention.

For each cardiac beat, Detected LV event data is collected within the duration of a data collection time interval 71. The data collection time interval 71 begins at a starting time point $T_S$ and ends at an ending time point $T_E$.

In ETC devices having pacing capability such as the pacemaker/ETC device 21 of Fig. 3B, the analyzing unit 64 of the system 60 of Fig. 5 and the

like, the initiation of the data collection time interval 71 is triggered by the detection of an RV event or by the delivering of a pacing pulse to the RV. However, in embodiments of the present invention in which no sensing and no pacing are performed in the RV, the initiation of the data collection time interval 71 is triggered by the detection of an RA event or by the delivering of a pacing pulse to the RA.

In ETC devices having no pacing capability such as the pacemaker/ETC device 24 of Fig. 4, the analyzing unit 74 of the system 70 of Fig. 6 and the like, the initiation of the data collection time interval 71 is triggered by the detection of an RV event. However, in embodiments of the present invention in which no sensing is performed in the RV, the initiation of the data collection time interval 71 is triggered by the detection of an RA event.

The duration of the time interval 71 is preset by the user or cardiologist before the beginning of the data collection period and does not change during the data collection. The duration of the time interval 71 is typically 100-150 milliseconds, however, other duration values of the data collection time interval 71 may be used. The duration of the data collection time interval 71 is set such that it is large enough to include the LV sensed events representing the myocardial depolarization wave under extreme cardiac conditions which may be encountered in a patient including, *inter alia*, various ranges of heart rates with or without ETC signal application, with or without pacing in both non-treated and drug treated patients. The duration of the data collection time interval 71 is selected such that it does not extend into the next heart beat cycle. Practically, the duration of the data collection time interval 71 may also be limited by the data storage capacity available in the memory unit of the pacemaker/ETC devices or the ETC devices disclosed in detail hereinabove.

The data collection time interval 71 is divided into N contiguous time bins 72 of equal duration. The double headed arrow 74 represents the duration of each of the time bins 72 (which is equal to $T_E - T_S$) . This set of time bins forms the basis for recording a plurality of histogram data sets. Each of the plurality of histogram data sets may be stored in the memory unit 44 of the pacemaker/ETC device 21 (Fig. 3B) or of the ETC device 24 (Fig. 4) or in the

memory unit 66 of the analyzing unit 64 of the system 60 (Fig. 5) or of the analyzing unit 74 of the system 70 (Fig. 6). Each histogram data set of the plurality of histogram data sets represents a cumulative time distribution histogram and includes a set of integer variables each representing the cumulative number of locally sensed LV events which were detected within a particular time bin of the N time bins 72 in a plurality of beat cycles belonging to a particular histogram data set. Each of the histograms represents data collected from a plurality of beat cycles having in common a unique set of conditions including a specific LV detection sensitivity level, the beat being paced or sensed beats, and the beats having been collected during a time period in which ETC signal delivery substantially affects myocardial depolarization wave conduction velocity or during a time period in which no ETC signal delivery occurred or the ETC delivery which did occur did not substantially affect the myocardial depolarization wave conduction velocity, and having a cycle length belonging to a particular class of cycle lengths as is disclosed in detail hereinbelow. Each particular cycle length class includes heart beats having a duration falling within predetermined range of cycle length durations.

Reference is now made to Fig. 8A which is a schematic diagram illustrating the general steps of a method for collecting time histogram data sets under various cardiac conditions and for determining one or more sets of alert window parameters and one or more detection parameter sets from the histogram data, in accordance with a preferred embodiment of the present invention.

The method includes the implanting of a data collecting device in a patient (step 76). The term data collection device of step 76 is used herein as a broad term describing a device capable of sensing and detecting depolarization events in at least two cardiac sites and of processing and storing data. The data collection device is capable of delivering ETC non-excitatory signals to the heart. Preferably (but not necessarily), the device may also be capable of pacing the heart as is known in the art. For example, the data collection device may include the implantable electrodes 22 operatively connected to the pacemaker/ETC device 21 of Fig. 3A or to the device 24 of Fig. 4. Alternatively, the data collection device may include the implanted leads 22 operatively

connected to the external analyzing unit 64 of the system 60 of Fig. 5 or to the external analyzing unit 74 of the system 70 of Fig. 6.

The method further includes obtaining the histogram data sets disclosed in detail hereinabove (step 78). The histogram data sets are obtained by using a plurality of different detection parameters or a plurality of different detection parameter sets depending, inter alia, on the type and complexity of the event detection method which is implemented by the data collection device. Different histogram data sets are obtained under different cardiac conditions such as, but not limited to, different heart rate ranges, artificially paced heart beats, and naturally occurring heart beats (sensed), artificially paced heart beats in the presence of on-going delivery of non-excitatory ETC signals and naturally occurring heart beats in the presence of the on-going delivery of non-excitatory ETC signals. These different conditions are disclosed in detail hereinafter.

The histogram data sets collected by the pacemaker/ETC device 21 may be stored in the memory unit 44 and telemetrically transmitted to the analyzing unit 23 (Fig. 3A) for processing. If the ETC device 24 of Fig. 4 is used for data collecting, the histogram data sets are stored in the memory unit 44 of the device 24. If the system 60 of Fig. 5 is used for data collection, the histogram data sets collected by the analyzing unit 64 are stored in the memory unit 66 for further processing. If the system 70 of Fig. 6 is used for data collection, the histogram data sets collected by the analyzing unit 74 are stored in the memory unit 66 for further processing.

The method further includes processing of the histogram data sets obtained in step 78 to determine one or more sets of alert window parameters, and one or more sets of detection parameters (step 80). Typically, each of the alert window parameter sets includes an alert window starting time value and an alert window ending time value. Each of the determined alert window parameter sets and detection parameter sets may be suitable for use under a particular combination of cardiac conditions such as a particular heart rate in a sensed or in a paced heart beat, and in the absence or presence of on-going delivery of non-excitatory ETC signals. Each particular set of alert window parameters may be associated with a particular set of detection parameters. However, in some

cases a common single set of detection parameters may be associated with some or with all of the sets of alert window parameters.

In other cases, a single common set of window parameters may be used for some or for all of the cardiac conditions disclosed hereinabove.

The method also includes the step of programming an implanted ETC device or ETC/pacemaker device with the determined set or sets of alert window parameters and with the determined set or sets of detection parameters (step 82).

It is noted that, the step 78 and the step 80 may or may not be performed by the same device. For example, in accordance with a preferred embodiment of the present invention, step 78 may be performed by an implanted device such as but not limited to the device 21 of Fig. 3A (or the implanted device 24 of Fig. 4) , the stored data may then be telemetrically transmitted to an external analyzing unit such as but not limited to the analyzing unit 23 of Fig. 3A, step 80 is then performed by the analyzing unit 23 and in step 82 the implanted device 21 of Fig. 3A (or the implanted device 24, of Fig. 4) is telemetrically programmed with the determined set or sets of alert window parameters and with the set or sets of detection parameters.

In accordance with another preferred embodiment of the present invention, step 78 may be performed by a device including implanted electrodes such as the implantable electrodes 22 which are operatively connected to an external device such as but not limited to the analyzing unit 64 of Fig. 5 (or the analyzing unit 74 of Fig. 6) and the data is stored in the memory unit 66 of the analyzing unit 64 (or of the analyzing unit 74). Step 80 is then performed by the analyzing unit 64 (or the analyzing unit 74). The implantable electrodes 22 are then disconnected from the analyzing unit 64 (or from the analyzing unit 74) and in step 82 an implantable ETC or ETC/pacemaker device such as but not limited to the device 21 of Fig. 3A (or the device 24 of Fig. 4) is connected to the implantable electrodes 22 and implanted in the patient. The programming (step 82) of the device 21(or the device 24) with the alert window parameter set of the or sets and with the detection parameter set(s) may be performed prior to the

implantation of the device 21 (or the device 24) within the patient or may be performed telemetrically after implantation of the device 21 (or the device 24).

Reference is now made to Figs. 8B and 8C which are schematic flow control diagrams illustrating the steps of a data collection method for collecting time histogram data sets in detail, in accordance with a preferred embodiment of the present invention.

The data collection program embedded within the pacemaker/ETC device 21 or the analyzing unit 64 starts by checking whether the user or operator has terminated the collection of data (step 90). The user (typically the cardiologist) may terminate data collection by a suitable command which is transmitted telemetrically to the pacemaker/ETC device 21 of the system 20, or input manually to the analyzing unit 64 of the system 60 through one of the user interface device(s) 69. Typically, the command may set a suitable flag or change the value of a variable which is checked by the program. However, other suitable methods for terminating data collection may be used. If the user did terminate data collection the data collection program ends (step 92). If the user did not terminate data collection, the program gets the current sensitivity level value **SL** (step 94). The sensitivity level variable **SL** may be an integer variable which can take any integer value selected from a group of integer numbers, each representing a particular sensitivity value available for use in the pacemaker/ETC device 21 or the analyzing 64. For example, if the event detection sensitivity is determined by the crossing of a single voltage threshold and the pacemaker/ETC device can have 8 different sensitivity levels, **SL** may be any integer in the range 1-8.

The data collection program checks whether the pacemaker paced (step 96). This is performed by checking the pacing data for the current beat cycle which is stored by the pacemaker/ETC device 21 or by the pacing program operating the processing unit 61 of the analyzing unit 64. If the pacemaker paced the data collection program sets the value of the logical parameter to **EV**=PACE to indicate a paced beat cycle (step 97) and transfers control to step 100. If the pacemaker did not pace, the data collection program checks whether the pacemaker sensed (step 98) this is performed by checking the

event sensing status data which is stored for the current beat cycle by the pacemaker/ ETC device 21 or by the pacing program operating the processing unit 61 of the analyzing unit 64. If the pacemaker sensed, the data collection program sets the value of the logical parameter to **EV**=SENSE to indicate a sensed beat cycle (step 99) and transfers control to step 100.

The data collection program then checks whether a premature ventricular contraction (PVC) was detected (step 100). The detection of a PVC is performed by the pacemaker/ ETC device 21 or by the pacing program operating the processing unit 61 of the analyzing unit 64. A PVC may be detected using the signals sensed in the RV. As is known in the art, PVC's may be identified by detecting two consecutive ventricular events without an atrial event therebetween. For example, PVC detection methods used in pacemakers operating in a DDD mode are suitable for use in the data collection method of the present invention. However, other methods suitable for PVC detection may also be used. PVC detection methods are well known in the art, are not the subject matter of the present invention and will therefore not be discussed in detail hereinafter.

If a PVC was detected the data collection program returns control to step 90 for avoiding collection of data for the current beat cycle. If a PVC was not detected, the data collection program gets the value of the variable **ETC** (step 101). The variable **ETC** is a logical variable which can have the values "on" and "off". When **ETC**=OFF the histogram represents data considered to be collected under conditions in which there was no practically substantial influence of the delivery of ETC signals on the cardiac conduction velocity. When **ETC**=ON the histogram represents data considered to be collected under conditions in which the delivery of ETC signals has substantial influence of on the cardiac conduction velocity. The detailed procedure of setting the value of the variable **ETC** and the criteria used to set the value of the variable **ETC** are disclosed in detail hereinafter.

The program then determines the cycle length category **CL** (step 102). **CL** is a variable representing the cycle length category which holds an integer

number in the range 1- **CLENGTH** , where **CLENGTH** is the number of cycle length categories.

The cycle length category is determined (step not shown) from the time interval between the current RV event detection and the previous RV event detection. This time interval is known in the art as the "R-R interval". The time of occurrence of detection of the current and previous RV events are stored in the memory of the pacemaker/ ETC device 21 of Fig. 3A or of the analyzing unit 64 of Fig. 5 as is known in the art.

The **CL** value of the current R-R interval is determined (steps not shown) by assigning the appropriate cycle length category **CL** depending on the current value of the R-R interval. The number of cycle length categories and the range of R-R interval lengths included in each of the cycle length categories are predetermined. For example, all R-R intervals having a value between 400 milliseconds and 449 milliseconds are assigned a first cycle length category variable value **CL** =1, all R-R intervals having a value between 450 milliseconds and 499 milliseconds are assigned a second cycle length category variable value **CL** =2, all R-R intervals having a value between 500 milliseconds and 549 milliseconds are assigned a third cycle length category variable value **CL** =3 and so forth.

It is noted that the above disclosed values of the ranges of the R-R intervals and **CL** values are given by way of example only and that the number of predetermined cycle length categories values **CL** which are selected and the selected ranges of the R-R intervals may be varied depending, *inter alia*, on the amount of memory available for data storage, the desired temporal resolution, the processing power of the processing unit 30 (Fig. 3A) or of the controller 40 (Fig. 4) and other practical considerations.

The program then selects a histogram to be updated **HIST(EV,CL,SL,ETC)** based on the current values of the variables **EV**,**CL**, **SL** and **ETC** and updates the number of beats contributing to the data accumulated in the selected histogram by increasing by one the value of a histogram beat counter **HC(EV,CL,SL,ETC)** associated with the selected histogram **HIST(EV,CL,SL,ETC)** ( step 105). It is noted that, the value of all the plurality of

histogram beat counters **HC(EV,CL,SL,ETC)** is set to zero at the start of the data collection procedure (step not shown). The program then sets the value of the variable **TIME** to zero (step 106) and starts a timer (step 108) which updates the value of the variable **TIME** representing the time from starting of the current RV event detection. The program then checks whether a threshold crossing has occurred (step 110). If a threshold crossing does not occur, the program checks whether the value of the variable **TIME** is equal to or larger than the value of the variable **MAXDELAY** ( step 112) wherein **MAXDELAY** is a constant value representing the longest delay between a detected RV event and a detected LV event value for which the LV event is registered in a histogram. The value of **MAXDELAY** is represented by the data collection time interval 71 of Fig. 7, and is equal to the number of bins 72 multiplied by the bin duration 74 (Fig. 7).

If the value of the variable **TIME** is not equal to or larger than the value of the variable **MAXDELAY**, the program returns control to step 110. If the value of the variable **TIME** is equal to or larger than the value of the variable **MAXDELAY**, the program returns control to step 90.

If a threshold crossing occurs, the program calculates **BINNUMBER** the serial number of the time bin 72 within which the threshold crossing occurred (step 114). The bin number is calculated by dividing the current value of the variable **TIME** by the constant **BINSIZE** representing the duration of the time bins (**BINSIZE** is represented as the double headed arrow 74 of Fig. 7) and rounding the result up to the nearest integer value. The program then increments the event count associated with the time bin who's number **BINNUMBER** was calculated by step 114 by adding one to the value of the variable **HIST[EV,CL,SL, ETC](BINNUMBER)** (step 116).

The program then stops sensing of the LV sensed signal for a blanking time period of **BLANK_T** (step 118). The blanking time period **BLANK_T** is used to prevent spurious event detection caused by LV events having multiple peaks. The program then checks whether the value of the variable **TIME** is larger than the value of the variable **MAXDELAY** (step 120). If the value of the variable **TIME** is not larger than the value of the variable **MAXDELAY**, the

program returns control to step 110. If the value of the variable **TIME** is larger than the value of the variable **MAXDELAY**, the program returns control to step 90.

As the cycle length of the patient's heart beats varies during the data collection time period depending on the state of exertion of the patient and since the detection sensitivity level is typically automatically changed by the pacemaker/ETC device as is disclosed in detail hereinafter, the different histogram data sets will include at the end of the data collection period the cumulative time distribution histogram data for each unique data set.

In order to collect enough data histograms in the shorter cycle lengths categories, the patient may be asked by the cardiologist or physician to engage in physical activity. In the cases where the data is collected by the implanted pacemaker/ETC device 21 of Fig. 3A, the physician may instruct the patient to engage in a suitable physical activity regimen once a day or at any other suitable frequency. If the data collection is done using the system 60, the physician or user may stop data collection, disconnect the leads 22 from the analyzing unit 64 and ask the patient to perform a suitable physical activity or exercise to increase his heart rate. The physician or user then reconnects the leads 22 to the analyzing unit 64 and continues the data collection.

Additionally, in order to get adequate data collection including sufficient data for both paced and sensed events, the pacemaker A-V delay may be changed. For example, when the data is collected by using the system 60 of Fig. 5, the A-V delay be changed by a physician during the data collection period, by reprogramming the value of the A-V delay using the user interface device(s) 69. In another example, when the data is collected by using the implanted pacemaker/ETC device 21 of Fig. 3A, once each night (by system clock) the sum of the histogram beat counters **HC(EV,CL,SL,ETC)** of all sensed histograms **HIST(EV,CL,SL, ETC)** having **EV=0** is computed to obtain a first sum representing the total number of sensed beats collected. The sum of the histogram beat counters of all paced histograms **HIST(EV,CL,SL,ETC)** having **EV=1** is also computed to obtain a second sum representing the total number of paced beats collected. The ratio of the first sum and the second sum is then

computed. If the computed ratio is smaller than a pre-selected lower limit such as, but not limited to, 1:20 (paced beats: sensed beats), the A-V delay is shortened. A-V delay shortening by approximately 20 milliseconds will typically lead to more paced beats. If the computed ratio is larger than a pre-selected upper limit such as, but not limited to 20:1 (paced beats: sensed beats), the A-V delay is lengthened by approximately 20 milliseconds for obtaining more sensed beats. In order to restrict the range of possible automatic modification of the A-V delay, high and low limits for A-V delay may be set. For example, a low A-V delay limit of 100 milliseconds and a high A-V delay limit of 300 milliseconds may be set but other different limit values may also be used.

Methods for adjusting the A-V delay of a pacemaker are known in the art. For example, U.S. patent 5,749,906 to Kieval discloses a method including adjustment of the A-V delay to achieve certain pacing conditions.

Alternatively, In cases were it is not possible to automatically adjust the A-V delay, if after the data was off-loaded, the user or the cardiologist finds that not enough data histograms for paced events were recorded, the A-V delay value of the pacemaker/ETC device may be shortened to increase the number of paced events and the patient may be sent away for an additional data collection period.

It is noted that the value of **SL** is set by an independent program (not shown). Various methods (not shown) for changing the detection sensitivity level may be used (not shown). Preferably, the value of **SL** is set to a number randomly selected from a group of numbers representing the available sensitivity levels of the pacemaker/ETC device. Alternatively, pseudo-random selection of the sensitivity level values may be used. Additionally, the method may use various forms of cycling of the sensitivity level. The rate of changing of the sensitivity level may be constant or variable. For example, the changing of the sensitivity level may be cyclic, pseudo-random or random, as long as data from enough beats is accumulated for each sensitivity level. The rate of change of the sensitivity level may be fixed, may change according to the time of day, or may be relatively rapid, such that data using the same sensitivity level would be recorded at different hours on different days. The latter rapid sensitivity change

method may be useful in view of the fact that patient's behavior is probably different at different times during the day.

Reference is now made to Fig. 9 which is a schematic graph illustrating a typical cumulative distribution of cardiac cycle length. The horizontal axis represents the cycle length in milliseconds and the vertical axis represents the number of occurrences accumulated over the sampling period for a particular cycle length. The curve 121 represents a typical cycle length cumulative distribution curve which is well known in the art. The data for such a curve may be collected over a sampling period of a few hours or a few days. It is noted that, while the overall cumulative distribution of cycle length may be similar to the exemplary curve 121 of Fig. 9, the longer cycle lengths are more frequent while sleeping (at night), and shorter cycles will be more frequent during working hours.

It is noted that when the pacemaker/ETC device 21 of Figs. 3 and 4 is used for collecting data, the amount of storage available on the memory unit 44 may be practically limited due to, *inter alia*, size, cost and current consumption of available memory units. This memory limitation may have to be taken into account with respect to the amount of histogram data that may be simultaneously stored in the memory 44. For example, turning briefly to Fig. 7, each of the bins 72 of the data collection time interval 71 may be allocated 3 bytes of memory space. The data collection time interval 71 may be divided into 100 bins 72, each of the bins 72 spanning a time interval 74 of 2 milliseconds. Twelve cycle length categories **CL** are pre-set. Each of the 12 cycle length categories **CL** is associated with cycle lengths falling into the twelve equal duration ranges 999-950 milliseconds, 949-900 milliseconds,..., 449-400 milliseconds. If eight different sensitivity levels **SL** are used and data is collected for paced and for sensed beat cycles and if a histogram header of 3 bytes is included in each histogram, the required amount of bytes that needs to be allocated for data histogram storage under such requirements is given by (3 X 100 + 3) X 12 X 8 X 2 = 58,176 bytes. If histogram data is also collected for sensed and paced beat cycles under ETC delivery conditions which are the

histograms **HIST[ EV, CL SL, ETC]** having **ETC** = ON , 116,352 bytes need to be allocated for histogram data storage.

Memory may be saved by using dynamic memory allocation techniques known in the art.

It is noted that, the particular cycle beat ranges (cycle length categories) disclosed hereinabove are given by way of example only and other different cycle-length categories having different cycle-length ranges may be used. Additionally, while the cycle length categories disclosed hereinabove have cycle length ranges of equal size, in other preferred embodiments of the present invention the data collection method may also use cycle length categories having non-identical R-R interval collection ranges. For example, all R-R intervals having a value between 400 milliseconds and 449 milliseconds may be assigned a first cycle length category variable value **CL** =1, all R-R intervals having a value between 450 milliseconds and 549 milliseconds are assigned a second cycle length category variable value **CL** =2, all R-R intervals having a value between 550 milliseconds and 669 milliseconds may be assigned a third cycle length category variable value **CL** =3 and so forth.

Reference is now made to Fig. 10 which is a schematic diagram illustrating the steps of the method of updating the value of the logical variable ETC of Figs. 8B-8C.

The method may be implemented as a software program which is executed in parallel with the program of Figs. 8B-8C. on the controller unit 40 of the pacemaker/ETC device 21 or on the processing unit 61 of the analyzing unit 64 or on any other suitable processing unit which is used for data collection in the present invention.

The program starts by setting the value of the logical variable **ETC** to **ETC** =OFF (step 130). The program then sets the value of the counter **ETC_COUNT** to zero (step 134). The program then checks whether an ETC signal was delivered during the current beat cycle (step 138). If an ETC signal was delivered during the current beat cycle, the program checks whether **ETC_COUNT** = **ETC_CHANGE** (step 142). **ETC_CHANGE** is a preset integer constant. The value of **ETC_CHANGE** is a fixed preset value. Typically, the

value of **ETC_CHANGE** is empirically found and may depend, *inter alia*, on the intensity, waveform shape, polarity and duration of the delivered ETC stimulation. Typically, the value of **ETC_CHANGE** may be in the range of approximately 2-8, For example, the value of **ETC_CHANGE** = 6 may be used. However, other values of the **ETC_CHANGE** may be used.

If an ETC signal was not delivered during the current beat cycle, the program checks whether **ETC_COUNT** = 0 (step146).

In step 142, if **ETC_COUNT** is equal to **ETC_CHANGE** control is transferred to step 158. If **ETC_COUNT** is not equal to **ETC_CHANGE** the program increments the current value of **ETC_COUNT** by one (step 150) and transfers control to step 158.

In step 146, if **ETC_COUNT** = 0, the program transfers control to step 158 and if **ETC_COUNT** is not equal to zero the program decrements the current value of **ETC_COUNT** by one (step 154) and transfers control to step 158.

In step 158 the program checks whether **ETC_COUNT** = **ETC_CHANGE**. If **ETC_COUNT** = **ETC_CHANGE**, the program sets the value of the parameter **ETC** to **ETC**=ON (step 162) and returns control to step 138. If **ETC_COUNT** is not equal to **ETC_CHANGE**, the program sets the value of the parameter **ETC** to **ETC** = OFF (step 166) and returns control to step 138. The program of Fig. 10 thus updates the value of the logical parameter ETC for the current beat cycle.

Ensuring acquisition of paced and sensed data

in order to collect data for all sensitivity level values for each cycle length value of paced and sensed events with and without ETC stimulation, the sensitivity level is automatically changed by the pacemaker/ETC device 21 or by the analyzing unit 64. The order of change might be cyclic, pseudo-random or random, as long as a sufficient number of beats is sampled for each sensitivity level. The rate of change of the sensitivity level may be fixed, changing relative to the time of day, or may be changed relatively fast, so that data collected with the same sensitivity level would be collected at different hours on different days, as the patients' behavior is probably different at different times during the day.

While the overall distribution of cycle length might be similar to Fig. 9, the longer cycle lengths are typically more frequent while sleeping (at night), and shorter cycle lengths are typically more frequent during working hours. Thus, preferably, the sensitivity level is randomly or pseudo-randomly changed every beat cycle to prevent biasing of the results due to time of day bias of cycle length.

Data processing and analysis methods

After enough data was collected by the data collection program of Figs. 8B-8C, the data is telemetrically off-loaded from the pacemaker/ETC device 21 to the analyzing unit 24 of the system 20 for further processing. Alternatively, if the system 60 has been used, the data is stored in memory unit 66 and is available for further processing by the processing unit 61.

Reference is now made to Figs. 11A and 11B which are schematic control flow diagrams of the main program implementing the method for analyzing acquired data histograms, in accordance with a preferred embodiment of the present invention.

The main program uses the data histograms collected as disclosed in hereinabove and illustrated in Figs. 7 and 8 to determine the alert window parameters under a variety of different cardiac conditions. The conditions include paced and sensed events, the absence and in the presence of ETC signals and a plurality of different cycle length ranges. The main program determines a set of appropriate alert window parameters and an appropriate amplifier sensitivity level for each of the above conditions.

The main program starts to analyze the collected data histograms for sensed events in the absence of ETC signal delivery by setting the value of the parameters **EV**, and **ETC** as follows **EV** = SENSE, **ETC**=OFF (step 170). The program then sets the value of the cycle length category parameter **CL** to **CL**=1 (step 172). The program then transfers control to a sensitivity level determining procedure for determining the appropriate sensitivity level **SL** for the particular histogram having **CL**=1 (step 174). The sensitivity level determining procedure is disclosed in detail hereinafter. The program then transfers control to a window position determining procedure for determining the alert window position

parameters **GROUPMIN** and **GROUPMAX** for the particular histogram having **CL** =1 (step 176). The parameters **GROUPMIN** and **GROUPMAX** are defined in detail hereinafter.

The main program then checks whether the current value of the cycle length category parameter **CL** is smaller than the number of the cycle length categories **CLENGTH** (step 178). For example, the total number of cycle length categories used in collecting the data may be twelve cycle length categories as in the non-limiting example given hereinabove (**CLENGTH** = 12) but other values of **CLENGTH** may be used according to the total number of cycle length categories used in collecting the data. If **CLENGTH** is greater than **CL**, the program increments the value of **CL** by 1 (step 180) and returns control to step 174 for determining the alert window parameters **SL**, **GROUPMIN** and **GROUPMAX** of the next cycle length category. If **CLENGTH** is not greater than **CL**, the program transfers control to step 182.

In step 182, the program proceeds to analyze the collected data histograms for sensed events in the presence of ETC signal delivery by setting the value of the parameters **EV**, and **ETC** as follows **EV** = SENSE, **ETC**=ON. The program then sets the value of the cycle length category parameter **CL** to **CL** =1 (step 184). The program then transfers control to the sensitivity level determining procedure for determining the appropriate sensitivity level **SL** for the particular histogram having **CL** =1 (step 186). The program then transfers control to the window position determining procedure for determining the alert window position parameters **GROUPMIN** and **GROUPMAX** for the particular histogram having **CL** =1 (step 188).

The main program then checks whether the current value of the cycle length category parameter **CL** is smaller than the number of the cycle length categories **CLENGTH** (step 190). If **CLENGTH** is greater than **CL**, the program increments the value of **CL** by 1 (step 192) and returns control to step 186 for determining the alert window parameters **SL**, **GROUPMIN** and **GROUPMAX** of the next cycle length category. If **CLENGTH** is not greater than **CL**, the program transfers control to step 194.

In step 194, the program proceeds to analyze the collected data histograms for paced events in the absence of ETC signal delivery by setting the value of the parameters **EV**, and **ETC** as follows **EV** = PACE, **ETC**=OFF. The program then sets the value of the cycle length category parameter **CL** to **CL** =1 (step 196). The program then transfers control to the sensitivity level determining procedure for determining the appropriate sensitivity level **SL** for the particular histogram having **CL**=1 (step 198). The program then transfers control to the window position determining procedure for determining the alert window position parameters **GROUPMIN** and **GROUPMAX** for the particular histogram having **CL** =1 (step 200).

The main program then checks whether the current value of the cycle length category parameter **CL** is smaller than the number of the cycle length categories **CLENGTH** (step 202). If **CLENGTH** is greater than **CL**, the program increments the value of **CL** by 1 (step 204) and returns control to step 198 for determining the alert window parameters **SL**, **GROUPMIN** and **GROUPMAX** of the next cycle length category. If **CLENGTH** is not greater than **CL**, the program transfers control to step 206.

In step 206, the program proceeds to analyze the collected data histograms for paced events in the presence of ETC signal delivery by setting the value of the parameters **EV**, and **ETC** as follows **EV** = PACE, **ETC**=ON. The program then sets the value of the cycle length category parameter **CL** to **CL**=1 (step 208). The program then transfers control to the sensitivity level determining procedure for determining the appropriate sensitivity level **SL** for the particular histogram having **CL** =1 (step 210). The program then transfers control to the window position determining procedure for determining the alert window position parameters **GROUPMIN** and **GROUPMAX** for the particular histogram having **CL**=1 (step 212).

The main program then checks whether the current value of the cycle length category parameter **CL** is smaller than the number of the cycle length categories **CLENGTH** (step 214). If **CLENGTH** is greater than **CL**, the program increments the value of **CL** by 1 (step 216) and returns control to step 210 for determining the alert window parameters **SL**, **GROUPMIN** and **GROUPMAX** of

the next cycle length category. If **CLENGTH** is not greater than **CL**, the program transfers control to the common window parameter determining procedure for computing a parameter set suitable for all cycle length categories and all cardiac conditions, based on the **SL**, **GROUPMIN** and **GROUPMAX** values computed for all the various cardiac conditions disclosed hereinabove (step 206).

After successful analysis of the available histogram data is completed by the main program the result may be an array or Look up table including the alert window parameter sets associated with each of the specific combinations of the parameters EV, CL, and ETC representing all the various cardiac conditions as disclosed hereinabove. Alternatively, the analysis may result in a single set of alert window parameters commonly used for all the various cardiac conditions as disclosed hereinabove.

Reference is now made to Fig. 12 which is a schematic flow control diagram illustrating the steps of the sensitivity level determining procedure used in the main program of Figs. 11A-11B. The sensitivity level determining procedure is used for determining the appropriate sensitivity level and the alert window parameters for a particular cycle length. The data histogram which was acquired using the lowest sensitivity level (the highest threshold for the specific exemplary case of using a single positive threshold level) is processed first. The sum of detected events recorded in the data histogram is compared to the expected cumulative number of detected events for the current data histogram (**TOTBEATS**). If not enough events were detected, this indicates that the sensitivity level was too low (the threshold is too high), and the data histogram acquired using the next (higher) sensitivity level is processed next.

Ideally, only events that are synchronized to the heart activity, namely the sensing of the ventricle beat in the LV, are supposed to be recorded in the data histograms. However, practically, various types of spurious events may be detected and included in the data histogram. Such spurious ("false") detected events may include electrical depolarization events associated with PVCs and non-random electrical noise peaks which are cyclic or almost cyclic in nature and therefore occur within the alert window period triggered by the RV. The

spurious detected events may also include lead movement artifacts which are likely to be synchronized to heart activity, and may therefore appear in a relatively stable position within the data collection time interval 71 of Fig. 7, and electrical Artifacts which are due to skeletal muscle activation which may or may not be synchronized with the cardiac cycle. Spurious detected events may also include polarization artifacts which are electrical noise generated by the activation of parts of the ventricle different from the ventricle's part or site at which the sensing is performed. When the heart is also paced, the spurious events may include pacing artifacts. During data acquisition, the detection time of the LV depolarization event may drift within the data collection time interval 71 because the detection of spurious events in the RV such as electrical noise, depolarization due to PVCs, and the like may lead to premature initiation of data acquisition in the data collection time interval 71.

In addition to the recording of spurious (false) events in the data histograms, it may also happen that a "true" event is not recorded in a data histogram even though a depolarization wave did occur in the RV, because the depolarization wave was not conducted to the LV.

If enough detected events are recorded in the data histogram, the procedure attempts to establish the alert window parameters. A suitable window may not be found if the sensitivity level was such that not all the actual events registered, but some noise did register as detected events. In such a case, the procedure may get enough events registered in the histogram, but the events will be spread out among the bins. In this case, the procedure will consider a higher sensitivity level. If the procedure succeeds in finding suitable alert window, the sensitivity level for the analyzed histogram is recorded, otherwise an appropriate error message is returned to inform the user of the failure to establish an appropriate alert window for the currently analyzed data histogram.

Thus, preferably, the beginning time point and the ending time point of the alert window are determined such that they are optimized for a predetermined level of LV event detection, while reducing the probability of spurious event detection.

If, for any of the above disclosed reasons, no adequate alert window was found (although there where more events recorded than actual beats happening), the next (higher) sensitivity level is processed. If no appropriate window is found for any of the sensitivity levels (of a particular combination of values of **CL**,**EV** and **ETC**, an error message is returned. The steps of the sensitivity level determining procedure are disclosed in detail hereinbelow.

The sensitivity level determining procedure starts by setting the value of the sensitivity level **SL** to **SL**=1 which is the lowest sensitivity level used for the detection (step 250). For example, if the detection method uses only a single positive threshold crossing criterion, the value **SL**=1 represents the highest voltage threshold level which was used in data collection. Similarly, if the detection method uses another different detection criterion or combination criteria **SL** =1 will represent the least sensitive detection criterion level or the least sensitive combination of detection criteria which in use will lead to the smallest number of detections, **SL**=2 will represent the second least sensitive detection criterion level or the second least sensitive combination of detection criteria and the last sensitivity level will represent the most sensitive detection criterion level.

The procedure then gets the data histogram array **HIST(EV,CL,SL,ETC)** (step 252). The procedure then computes the value of the variable **TOTBEATS** for the current histogram **HIST(EV,CL,SL,ETC)** by multiplying the preset parameter **P** by the value of the histogram beat counter **HC(EV,CL,SL,ETC)** (step 254). The variable **TOTBEATS** represents the expected cumulative number of detected events for the current data histogram **HIST(EV,CL,SL,ETC)**. The value of histogram beat counter variable **HC(EV,CL,SL,ETC)** is the actual number of beats included in the recorded data histogram **HIST(EV,CL,SL,ETC)** (see step 105 of Fig. 8C). The parameter **P** is a preset parameter representing the desired minimum probability of event detection (assuming no noise is present). For example, if the preset desired minimum probability of event detection is **P**=0.98 and the current histogram **HIST(EV,CL,SL,ETC)** includes data recorded from 100,000 heart beats, the computed value is **TOTBEATS** = 0.98X100,000 = 98,000 detected events.

The procedure then transfers control to a procedure for computing and returning the value of the variable **HIST_SUMBIN** (step 256). The steps of the procedure for computing the value of the variable **HIST_SUMBIN** are disclosed in detail hereinafter (see Fig. 14). Briefly, the variable **HIST_SUMBIN** represents the total sum of the number of detected events which are recorded in all the bins 72 of the data collection time interval 71 (Fig. 7) and which are stored in the current data histogram **HIST(EV,CL,SL,ETC)**. The procedure then checks whether the current value of **HIST_SUMBIN** is larger than the value of the parameter **TOTBEATS** (step 258).

If the current value of **HIST_SUMBIN** is not larger than the value of the computed parameter **TOTBEATS**, indicating that the desired value of **TOTBEATS** is not achievable using the current sensitivity level **SL**, the procedure increments the value of the parameter **SL** by 1 (step 260) and transfers control to step 252. If the current value of **HIST_SUMBIN** is larger than the value of the computed parameter **TOTBEATS**, this indicates that the desired value of **TOTBEATS** is achievable using the current sensitivity level **SL**, and the procedure transfers control to the window position determining procedure (step 262).

The procedure then checks the output returned by the window position determining procedure (step 264). If the window position determining procedure returned the value "OUTPUT OK", the procedure updates the variable **SENS(EV, CL, ETC)** which represents the appropriate sensitivity level for cycle length category **CL**, the current event variable **EV**, and the current excitable tissue control variable ETC, by setting **SENS(EV,CL,ETC)=SL** (step 266) and returns control to the main program (step 274). If the window position determining procedure did not return the value "OUTPUT OK", the procedure checks whether **SL< SLEVELS** (step 268). If the current sensitivity level value **SL** is smaller than the number of sensitivity levels **SLEVELS**, the procedure increments the value of **SL** by 1 (step 270), and returns control to step 262. If the current sensitivity level value **SL** is not smaller than the number of sensitivity levels **SLEVELS**, the procedure returns an error message "ERROR IN WINDOW PLACEMENT" (step 272) and returns control to the main program

(step 274). In such a case the data set is not considered adequate for generating a complete set of alert window parameters.

Reference is now made to Figs. 13A-13C which are schematic flow control diagrams illustrating the steps of the window position determining procedure used in Figs. 11A, 11B and in Fig. 12.

The window position determining procedure of Figs. 13A-13C is used to determine the alert window parameters. The procedure returns for each histogram **HIST(EV,CL,SL,ETC)**, a pair of values, representing the starting (earliest) bin number and the ending (latest) bin number of the alert window appropriate for the current histogram. These pairs of starting and ending bin numbers are stored in an array **WINDOW(EV, CL,ETC)** in which array, for each specific combination of cycle length category value **CL**, **EV** value, and **ETC** value there are stored a pair of integer numbers representing the starting bin number and the ending bin number for the alert window determined based on the analysis of the data histogram **HIST(EV,CL,SL,ETC)** having this specific combination **CL**, **EV** and **ETC** values.

The window position determining procedure starts by sorting the bins of the current histogram **HIST(EV,CL,SL,ETC)** (step 300). Generally, the number of events recorded in the group of bins constituting an alert window should be at least **TOTBEATS** events and the number of bins within any alert window is limited to **MAXWIN** bins. The bin sorting step 300 may be performed by sorting the bins in descending order of bin value wherein the bin value is the number of events accumulated in a particular bin. The sorting of step 300 may be accomplished by any suitable sorting method such as a heap sort, a bubble sort or by any other suitable sorting method known in the art. Thus, the step 300 results in a sorted list of bins. Next, the procedure finds the number **N** which is the minimum number of bins containing more than **TOTBEATS** of recorded events by going to the **N** determining procedure and returning a value for **N** (step 302).

The procedure then compiles a bin list **NLIST** including the first **N** bins within the current histogram (step 304). The procedure then sorts the list **NLIST** by ascending bin number (step 306). The sorting method may be similar to the

sorting method used in step 300 hereinabove except that the sorting is performed according to bin number and not according to the bin value. However, any other suitable sorting method known in the art may be used in step 306.

The procedure then sets the value of an integer group counter **m** to **m=1** (step 308). The procedure thus defines first a bin group **GROUP(1)** of a number of bin groups **GROUP(m)**. The procedure sets to zero the value of the parameter **GROUPSIZE(m)** which represents the number of bins currently included in the bin group **GROUP(m)** (step 309). The procedure stores the value of the bin number of the first bin on the list **NLIST** in the variable **TEMPBIN** (step 310). The procedure then adds the bin number **TEMPBIN** of the first bin on **NLIST** as the first bin number of the bin group **GROUP(m)** and removes the bin number **TEMPBIN** from the bin list **NLIST** (step 312). The procedure then increments the value of the parameter **GROUPSIZE(m)** by 1 (step 313). The procedure then checks whether **NLIST** is empty (step 314). If **NLIST** is empty, there is only one group of bins containing one bin and the procedure updates the parameter **GROUPNUMBER** representing the current number of groups by setting **GROUPNUMBER =m** (step 315), and transfers control to the group sorting procedure of step 330 for group sorting. If **NLIST** is not empty, the procedure proceeds by storing the number of the next bin after **TEMPBIN** in the list **NLIST** in the variable **NEXTBIN** (step 316). The procedure then checks whether the current first bin in the list NLIST is adjacent to the last bin added to the current bin group **GROUP(m)**, by checking whether **NEXTBIN =TEMPBIN +1** ( step 318). If the value of **NEXTBIN** is not equal to **TEMPBIN +1**, this indicates that the bins are not adjacent bins and the procedure opens a new bin group by incrementing the value of the group counter **m** by 1(step 320), resets the value of **GROUPSIZE(m)** to zero (step 321), stores the current value of **NEXTBIN** in **TEMPBIN** (step 322) and returns control to step 312 for generating the next bin group.

If **NEXTBIN =TEMPBIN +1**, this indicates that the bins are adjacent bins and the procedure stores the current value of **NEXTBIN** in **TEMPBIN**, adds the bin number **NEXTBIN** to the current bin group **GROUP(m)** and removes the bin

number **NEXTBIN** from the list **NLIST** (step 324). The procedure then increments the value of the parameter **GROUPSIZE(m)** by 1 (step 326) and returns control to step 314.

In this way, the procedure generates one or more bin groups, each of these groups including contiguously adjacent bins, until the list **NLIST** is empty.

The group sorting procedure of step 330 is disclosed in detail hereinafter (and illustrated in Fig. 16 hereinbelow). Briefly, the total number of events in each bin group is determined and the groups are then sorted by descending total number of group events.

After sorting the bin groups for the current histogram, the procedure begins processing the bin group having the largest number of recorded events by setting a group index L to a value of L=1 (step 332). The group index **L** represents the position of the bin group within the sorted list **NLIST**. The procedure then checks whether **GROUPSUM(L)** ≥ **TOTBEATS**, wherein **GROUPSUM(L)** is the sum of the number of events recorded in all the bins in bin group **GROUP(L)**, and **TOTBEATS** is the expected cumulative number of detected events for the current data histogram **HIST(EV,CL,SL,ETC)** (step 334). If **GROUPSUM(L)** is smaller than **TOTBEATS**, the procedure gets the values of **GROUPMIN** and **GROUPMAX** for **GROUP(L)** (step 336). These values were found by the group sorting procedure (see Fig. 16) as is disclosed in detail hereinafter. The procedure then checks whether the current group spans the entire histogram length by checking whether **GROUPMIN** =1 and **GROUPMAX** = **MAXBINS**, wherein **MAXBINS** is the total number of bins in the histogram (step 338). If **GROUPMIN** =1 and **GROUPMAX** = **MAXBINS**, this means that the current group includes all the bins in the entire histogram. However, since in step 334 the procedure determined that the total number of events recorded in the bins of the current group is smaller than the expected total number of events for the entire histogram, a contradiction is indicated and the procedure evokes an error message "NOT OK" (step 340) and returns control to the main program (step 342).

If, in step 338 **GROUPMIN** is not equal to 1 or **GROUPMAX** is not equal to **MAXBINS**, the procedure transfers control to the group enlarging procedure

for enlarging **GROUP(L)** (step 344) as is disclosed in detail hereinafter (see Fig. 18) and returns control to step 334.

Going back to step 334, if **GROUPSUM(L)** is equal to or larger than **TOTBEATS**, the procedure transfers control to the group shrinking procedure for shrinking **GROUP(L)** (step 346) as is disclosed in detail hereinafter (see Fig. 17). After control is returned by the group shrinking procedure, the procedure checks whether **GROUPSIZE(L)>MAXWIN(EV,CL,ETC)**, wherein **MAXWIN(EV,CL,ETC)** is an array or a look-up table (LUT) including values representing the maximal window size (in bins) which is considered to be the maximal acceptable window size for a specific combination of values of the parameters **CL, EV** and **ETC**. Thus, for example, the value stored in the position **MAXWIN(1,PACE,ON)** of the array or LUT **MAXWIN(EV,CL,ETC)** represents the maximal acceptable window size for a paced beat having a cycle length falling in the first cycle length category and having a logical variable **ETC**=ON. In another example, the value stored in the position **MAXWIN(3, SENSE, OFF)** of the array or LUT **MAXWIN(EV, CL, ETC)** represents the maximal acceptable window size for a sensed beat having a cycle length falling within the third cycle length category and having a value of the logical variable **ETC**=OFF.

The values stored in the array or LUT **MAXWIN(EV, CL, ETC)** are empirically found values which are typically preset before the data processing by the main program is begun. These values may be based, *inter alia*, on clinical results previously obtained in a plurality of patients and on considerations involving a compromise between alert window size and acceptable spurious noise levels.

It will be appreciated that some of the values stored in the array or LUT **MAXWIN(EV,CL,ETC)** may be identical. For example, in accordance with one preferred embodiment of the present invention, the values representing the maximal acceptable window size for a plurality of cycle length categories may be the same. Thus, the array or LUT **MAXWIN(EV, CL, ETC)** may be partially "degenerate". In accordance with another preferred embodiment of the present embodiment, the array or LUT **MAXWIN(EV, CL, ETC)** may be completely degenerate, in which case it is replaced by a single constant **MAXWIN**

representing a maximal window size acceptable under all cardiac conditions and the check performed in step 348 becomes a check whether **GROUPSIZE(L)>MAXWIN** (this step is not actually shown in Fig. 13B).

If **GROUPSIZE(L)>MAXWIN(EV,CL,ETC)**, the procedure checks whether **L=GROUPNUMBER** (step 350). If **L=GROUPNUMBER,** this indicates that there are no more available bin groups left and that the available collected data does not allow assigning for the current histogram an alert window size which is equal to or smaller than the maximal acceptable window size and the procedure returns an error message "not OK" (step 340) and returns control to the main program (step 342)

If **L** is not equal to **GROUPNUMBER**, this indicates that there are bin groups left to be analyzed and the procedure increments the value of **L** by 1 (step 352) and returns control to step 334 for further processing of additional bin group data.

Going back to step 348, if **GROUPSIZE(L)** is equal to or smaller than the current value of **MAXWIN(EV,CL,ETC),** this indicates that the size of the current group is acceptable as the size of the alert window and the procedure stores the current values of **GROUPMIN** and **GROUPMAX** as the appropriate pair of values representing the starting (earliest) bin number and the ending (latest) bin number of the alert window, respectively, appropriate for the current histogram in the array **WINDOW (EV,CL,ETC)** (step 354), the procedure returns an "OK" message (step 356) and transfers control to the procedure or program from which it was invoked (step 342).

Reference is now made to Fig. 14, which is a schematic flow diagram representing the steps of a procedure for determining the sum of the number of detected events stored in a given data histogram, in accordance with a preferred embodiment of the present invention.

The procedure starts by setting the value of an integer counter **T** to **T=1** (step 360). The counter **T** represents the number of the current bin within the current data histogram **HIST(EV, CL,SL,ETC)**. The procedure also sets the value of an integer bin counter **S** to **S=0** (step 362). The procedure then increments the current value stored in the bin counter **S** by the number

**HIST(EV, CL,SL,ETC)(T)** representing the number of detected events stored in bin **T** of the current data histogram **HIST(EV, CL,SL,ETC)** (step 364). The procedure then checks whether **T=MAXBINS** (step 366), wherein **MAXBINS** is the total number of bins in the current data histogram **HIST(EV,CL,SL,ETC)**. If **T** is not equal to **MAXBINS**, the procedure increments the value of **T** by 1 (step 368) and transfers control to step 364. If **T=MAXBINS**, the procedure stores the current value of **S** as the value of **HIST_SUMBIN** (step 370) and returns control to the sensitivity level determining procedure of Fig. 12.

Reference is now made to Fig. 15 which is a schematic flow control diagram illustrating the steps of a procedure for determining the value of the variable **N** usable in the window position determining procedure of Figs. 13A-13C, in accordance with a preferred embodiment of the present invention.

The procedure of Fig. 15 starts setting the value of an integer counter **T** to **T=1** (step 372). The counter **T** represents the number of the current bin within the current data histogram **HIST(EV, CL,SL,ETC)**. The procedure also sets the value of an integer bin counter **S** to **S=0** (step 374). The procedure then increments the current value stored in the bin counter **S** by the number **HIST(EV, CL,SL,ETC)(T)** representing the number of detected events stored in bin **T** of the current data histogram **HIST(EV, CL,SL,ETC)** (step 376). The procedure then checks whether **S≥TOTBEATS** (Step 378). If **S** is not larger than or equal to **TOTBEATS** the procedure increments the value of **T** by 1 (step 380) and transfers control to step 376. If **S** is larger than or equal to **TOTBEATS** the procedure stores the current value of **T** as the value of **N** (step 382) and returns control to the window position determining procedure of Figs. 13A-13C.

Reference is now made to Fig. 16 which is a schematic flow control diagram illustrating the steps of the group sorting procedure usable in the window position determining procedure of Fig. 13B, in accordance with a preferred embodiment of the present invention.

Briefly, the group sorting procedure sorts the groups obtained for the current data histogram by computing the total number of detected events stored in all the bins included within each of the groups of the current data histogram

group **GROUP(T)**, stores the obtained group event sums in an array **GROUPSUM(T)** and then sorts the groups by sorting the values within the array **GROUPSUM(T)** by descending order of total group event number.

The procedure sets the value the value of an integer group counter **T** to **T=1** (step 390). The group counter **T** represents the number of the current bin group **GROUP(T)**. The procedure also sets the value of an integer group event counter **S** to **S=0** (step 392). The procedure stores in an integer variable **M** the value of the variable **GROUPMIN** representing the minimal bin number included in the current **T**'th group **GROUP(T)**, stores in the pointer **TEMPBIN** the number of detected events which is stored in the first bin of the current bin group **GROUP(T)**, and stores in an integer variable **L** the value of the variable **GROUPMAX** representing the maximal bin number included in the current **T**'th group **GROUP(T)** (step 394). The group sorting procedure then updates the value of the group event counter **S** by adding the current value of **TEMPBIN** to **S** (step 396). The procedure then checks whether **M=L** (step 398). If **M** is not equal to **L**, indicating that there are additional bins within the current group **GROUP(T)**, the procedure increments the value of **M** by 1 and stores the number of events stored in the **M**'th bin of **GROUP(T)** in **TEMPBIN** (step 400), and transfers control to step 396.

If **M** is equal to **L**, indicating that there are no remaining bins within the current group **GROUP(T)**, the procedure stores the current value of group event counter **S** in the variable **GROUPSUM(T)** representing the total sum of the events detected in all the bins included in the current group **GROUP(T)** (step 402). The procedure then checks whether **T=GROUPNUMBER** (step 404). If the group counter **T** is not equal to **GROUPNUMBER**, indicating that not all the groups for the current data histogram have been processed, the procedure increments the value of the group counter **T** by 1 (step 406) and transfers control to step 392 for further group processing. If **T=GROUPNUMBER**, indicating that all the groups obtained for the current data histogram have been processed, the procedure sorts the values stored in the array **GROUPSUM(T)**, in descending order(step 408) and returns control to the window position determining procedure (of Fig. 13B).

Reference is now made to Fig. 17 which is a schematic flow control diagram illustrating the steps of the group enlarging procedure usable in the window position determining procedure of Fig. 13B, in accordance with a preferred embodiment of the present invention. As disclosed hereinabove (in step 334, 336 and 338 of Fig. 13B), the group enlarging procedure is used to enlarge a bin group in cases in which the current group includes less than **TOTBEATS** detected events. The current bin group is enlarged by consecutively adding bins to the group for increasing the total number of detected events included in the current bin group.

The group enlarging procedure of Fig. 17 starts by checking whether **GROUPMIN** =1 (step 420). If **GROUPMIN** =1, indicating that the first bin in the current group is identical to the first bin of the current data histogram, the procedure transfers control to step 428. If **GROUPMIN** is not equal to 1, indicating that the first bin in the current group is not identical to the first bin of the current data histogram, the procedure checks whether **GROUPMAX=MAXBINS** (step 422). If **GROUPMAX=MAXBINS**, the procedure decrements the value of **GROUPMIN** by 1 to add an additional bin to the group and updates the value of **GROUPSUM(L)** by adding to it the number of detected events **BIN(GROUPMIN)** stored in the bin which was added to the group (step 424). The procedure then returns control to the window position determining procedure of Fig. 13B.

If **GROUPMAX** is not equal to **MAXBINS**, the procedure checks whether **BIN(GROUPMAX+1)≥BIN(GROUPMIN-1)** (step 426), wherein **BIN(GROUPMAX+1)** represents the number of detected events stored in the bin of the current data histogram which is adjacent to the last bin of the current bin group and which is not included in the current bin group, and **BIN(GROUPMAX-1)** represents the number of detected events stored in the bin of the current data histogram which is adjacent to the first bin of the current bin group and which is not included in the current bin group. The check of step 426 is performed in order to determine on which side of the current group the next bin is to be added to the group based upon a comparison of the number of

detected events stored in the two bins which are adjacent to the current first and last bins of the current group.

If **BIN(GROUPMAX +1)** is not equal to or larger than **BIN(GROUPMIN-1)**, the procedure transfers control to step 424.

If **BIN(GROUPMAX +1)≥BIN(GROUPMIN-1)**, the procedure increments the value of **GROUPMAX** by 1 to add an additional bin to the group and updates the value of **GROUPSUM(L)** by adding to it the number of detected events **BIN(GROUPMAX)** stored in the bin which was added to the group (step 428) and returns control to the window position determining procedure of Fig. 13B.

Reference is now made to Fig. 18 which is a schematic flow control diagram illustrating the steps of the group shrinking procedure usable in the window position determining procedure of Fig. 13B, in accordance with a preferred embodiment of the present invention. The group shrinking procedure is invoked by step 334 of the window position determining procedure disclosed hereinabove (Fig. 13B) in cases in which the number of events in the current bin group is equal to or larger than **TOTBEATS**. The purpose of the group shrinking procedure is to remove from the current bin group bins in which the number of detected events is zero, the removal is performed starting from the bins positioned at the edges of the bin group and proceeds until a bin with a non-zero number of detected events is encountered.

The group shrinking procedure starts by checking whether the number of detected events **BIN(GROUPMIN)** which is stored in the current first bin of the current bin group is equal to zero (step 440). If **BIN(GROUPMIN) = 0**, the procedure removes the "empty" bin from the group by incrementing the value of the first bin number **GROUPMIN** by 1 (step 442) and returns control to step 440 for checking the next bin. If **BIN(GROUPMIN)** is not equal to zero, the bin is not empty and the procedure transfers control to step 444 for checking the last bin of the group. In step 444 the procedure checks whether the number of detected events **BIN(GROUPMAX)** which is stored in the current last bin of the current bin group is equal to zero. If **BIN(GROUPMAX) = 0**, the procedure removes the empty bin from the group by decrementing the value of the last bin number **GROUPMAX** by 1 (step 446) and returns control to step 444. If

**BIN(GROUPMAX)** is not equal to zero, the last bin is not empty, the group cannot be further shrunk and the procedure returns control to the window position determining procedure of Fig. 13B (step 448).

Reference is now made to Fig. 19 which is schematic flow control diagram illustrating the steps of the common window position parameters determining procedure usable in the main data analysis program of Figs. 11A -11B, in accordance with a preferred embodiment of the present invention. The purpose of the procedure illustrated in Fig. 19 is to analyze the values of the first and last window bin numbers which were computed from all the data histograms as disclosed hereinabove and which are stored in the array **WINDOW(EV,CL,ETC)** and to determine therefrom a set of parameters which may be stored in the memory of the ETC and pacemaker/ETC devices of the present invention and used for real time determination of the alert window timing parameters. The parameters determined by the procedure of Fig. 19 may represent the starting bin number and the ending bin number of a single fixed alert window also referred to as "static alert window" which will be used for all beats irrespective of the beat cycle length. This single set of static alert window parameters will be used for sensed beats (naturally occurring beats) and for paced beats, in the presence and in the absence of the delivery of ETC signals. The details of the use of a static alert window are disclosed in detail in International Application No. PCT/IL00/00126 Titled "APPARATUS AND METHOD FOR TIMING THE DELIVERY OF NON-EXCITATORY ETC SIGNALS TO A HEART".

In contrast to using a single set of alert window parameters, the starting time point and the duration of the alert window may be varied for beats having different cycle length (different R-R intervals). The method of adapting the parameters of the alert window (starting time point and ending time point) to the current cardiac conditions is referred to as the "dynamic alert window" method hereinafter.

The parameters determined by the procedure of Fig. 19 may be a set of approximation parameters which are used to compute in real time the alert window parameters. One simple way to determine the beginning and the ending time points for the alert window based on the current known value of the

R-R interval and of the value of the current values of the variables **EV** and **ETC**, as determined in real time, is to determine into which cycle length category **CL** the current R-R interval falls and to use the determined value of the alert window parameters (the starting and ending bin numbers) which are stored in the array **WINDOW(EV,CL,ETC)** to compute the starting and ending time points of the alert window based on the known bin duration. The advantage of such a method is that it is simple to implement. The computing of such an approximation may be advantageous due to the fact that the data recorded in a data histogram was actually derived from a plurality of beats having various different cycle lengths. Thus, while the data within a data histogram is used for computing an "average" common set of alert window parameters from all the beat cycles having a duration falling within the duration limits of a particular arbitrarily chosen cycle length category, the use of such a common set of alert window parameters for real time determining of the alert window delay and duration for all the beats falling within the cycle length category may result in non-optimal placement of the alert window, particularly for those beats having a cycle length value which is close to the "ends" of the cycle length category values (these ends are the shortest and longest beat cycle duration values which are still included within a particular cycle length category). This non-optimal alert window placement may be tolerated in cases in which a relatively large number of cycle length categories is used for data acquisition. However, in some preferred embodiments of the present invention it may be impractical or undesirable to use a large number of cycle length categories due to data capacity limitations of the memory of an implanted ETC or ETC/pacemaker device, or due to the need to acquire a larger number of cardiac beats in order to have enough data acquired for each of the cycle length category leading to an increase in the overall time period required for patient data acquisition. Therefore, in accordance with another preferred embodiment of the present invention, the alert window parameters stored in the array **WINDOW(EV,CL,ETC)** may be further processed to provide a set of approximation parameters which may be stored in the ETC or pacemaker/ETC device and used to compute in real time improved approximated values of the

beginning time point and the ending time point based on the current value of the R-R interval. The advantage of this approximation method is that it provides improved on-line computed approximations of the alert window beginning and ending time points while not overly increasing the necessary number of cycle length categories used for data acquisition, which may also be advantageous in shortening the time period required for collecting the histogram data sets from the patient.

The common window position parameters determining procedure of Fig. 19 starts by determining the values of the variables **MAXWINBEG** and **MAXWINEND** (step 500). As disclosed hereinabove, the array **WINDOW (EV,CL,ETC)** stores a plurality of pairs of bin numbers. The first number within each pair of bin numbers represents the number of the first bin (the bin at the window's beginning of the alert window determined for a particular combination of the variables **EV,CL,ETC** as disclosed in detail hereinabove), and the second number within each pair of bin numbers represents the number of the last bin (the bin at the window's end) of the same alert window. The variable **MAXWINBEG** is the difference between the highest first bin number and the lowest first bin number of all the first bin numbers of all of the pairs of bin numbers stored in the array **WINDOW (EV,CL,ETC)**. The variable **MAXWINBEG** therefore represents the maximal difference (in bins) between all the alert window beginning points included in the array the **WINDOW (EV,CL,ETC)**.

The variable **MAXWINEND** is the difference between the highest second bin number and the lowest second bin number of all the second bin numbers of all of the pairs of bin numbers stored in the array **WINDOW (EV,CL,ETC)**. The variable **MAXWINEND** therefore represents the maximal difference (in bins) between all the alert window ending points included in the array the **WINDOW (EV,CL,ETC)**.

Determining the values of **MAXWINBEG** and **MAXWINEND** may be performed in various ways. For example, in accordance with one non-limiting example, this may be performed by sorting the window beginnings (the first bin numbers of all the bin number pairs) by ascending bin number, then taking the

difference between the last and the first bin numbers of the sorted list to obtain **MAXWINBEG**. Similarly, sorting the window endings (the second bin numbers of all the bin number pairs) by ascending bin number, then taking the difference between the last and first bin numbers of the sorted list to obtain **MAXWINEND.**

Alternatively, in accordance with another non-limiting example, one may define a minimum beginning variable and a maximum beginning variable, both equal to the first (beginning) bin number of the first pair of bin numbers in **WINDOW(CL,EV,ETC)**, and then running through all the other bin number pairs, updating the value of the minimum beginning variable and the maximum beginning variable numbers if needed until all the bin number pairs in the array **WINDOW(CL,EV,ETC)** are exhausted. The difference between the maximum beginning variable value and the minimum beginning variable value then gives the value of **MAXWINBEG**. The value of **MAXWINEND** is computed by defining a minimum ending variable and a maximum ending variable both equal to the second (ending) bin number of the first pair of bin numbers in **WINDOW(CL,EV,ETC)**, and then running through all the other bin number pairs, updating the value of the minimum ending variable and the maximum ending variable numbers if needed until all the bin number pairs in the array **WINDOW(CL,EV,ETC)** are exhausted. The difference between the maximum ending variable value and the minimum ending variable value then gives the value of **MAXWINEND**.

It is noted that the values of **MAXWINBEG** and **MAXWINEND** may also be determined by any other suitable method or algorithm known in the art.

After determining the values of **MAXWINBEG** and **MAXWINEND**, The procedure continues by comparing the values of **MAXWINBEG** and **MAXWINEND** to the value of a user determined constant **MAXSHIFT** which represents the maximal allowable value (in bins) of **MAXWINBEG** and **MAXWINEND** (step 502). If **MAXWINBEG>MAXSHIFT** or **MAXWINEND>MAXSHIFT** indicating the maximal allowable value has been exceeded, the procedure sets the value of the flag **DFLAG** to 1 (step 504) , transfers control to a procedure for determining real-time window approximation parameters (step 506) and returns control to the main data analysis program

(Fig. 11B). If **MAXWINBEG** is not larger than **MAXSHIFT** and **MAXWINEND** is not larger than **MAXSHIFT,** the procedure sets the value of the flag **DFLAG** to zero (step 508), stores the value of **MINBEG** and **MAXEND** as the first bin number and the last bin number of **TOT_WINDOW** (step 510), wherein **TOT_WINDOW** is an array holding two window parameters representing the overall (unified) alert window, **MINBEG** represents the lowest value of the first (beginning) bin number of all the pairs of bin numbers stored in the array **WINDOW(CL,EV, ETC)**, and **MAXEND** represent the highest value of the second (ending) bin number of all the pairs of bin numbers stored in the array **WINDOW(CL,EV, ETC)**.

The procedure then sets an overall sensitivity level **SENS_LEVEL** for use in conjunction with the window parameters stored in **TOT_WINDOW,** by selecting the value of the highest sensitivity level determined **MAX[SENS(CL,EV,ETC)]** for any of the analyzed data as the value of **SENS_LEVEL** (step 512). For example, this may be accomplished by sorting by ascending or descending order all the sensitivity levels **SENSE(EV,CL,ETC)** determined by the sensitivity level determining procedure of Fig. 12 procedure during the performance of the main data analysis program of Figs. 11A and 11B, and by setting the last value or the first value, respectively, in the sorted list of sensitivity level values as the value of **SENS_LEVEL**. After setting the value of **SENS_LEVEL**, the procedure returns control to the main data analysis program of Fig. 11B (step 514).

The value of **SENS_LEVEL** and the array **TOT_WINDOW** are later telemetrically or non-telemetrically programmed into the memory unit (not shown) of the implantable ETC device 19 of Fig. 3A or into the memory unit 44 of the devices 21 or 24 (of Figs. 3A and 4, respectively) and is used in the operation of the devices 19, 21 and 24 for setting the beginning and ending points of the alert window and the detection sensitivity level, respectively, of the devices 19 or 21 or 24 in real-time as disclosed in detail hereinafter.

It is noted that, the value of **MAXSHIFT** is entered as input by the user (typically the cardiologist performing the data analysis) during the analysis, and may be based on the user's judgment of the duration of allowable common

(unified) alert window which will result in the a alert window which is large enough to include most of the events which need to be detected while still being positioned such as not to result in unacceptable levels of detection of spurious events due to electrical noise (synchronous or non-synchronous with the heart beat), PVCs, and the like. The user's decision about the appropriate value of **MAXSHIFT** may be assisted by visually observing the temporal distribution of detected events within the various data histograms which the user may display on the display unit 32 of the analyzing unit 23 of the system 20 (Fig. 3A) or of the system 60 (Fig. 5) and the system 70 (Fig. 6). The entry of the value of **MAXSHIFT** may be performed through a suitable user interface such as, but not limited to, one or more of the user interface(s) 31 of Fig. 3A, or one or more of the user interface device(s) 69 of Figs. 5 and 6.

Reference is now made to Fig. 20 which is a schematic graph useful for understanding a method for computing a set of approximation parameters for the real time computing of the alert window parameters, in accordance with a preferred embodiment of the present invention. The vertical axis represents the cycle length in arbitrary units and the horizontal axis represents the time measured from the detection of an RV event (the zero time point of the horizontal axis represents the time of detection of an RV event. This zero time point of the horizontal axis coincides with the time of detection of the RV event 11 of Fig. 2. The horizontal lines labeled 521, 522, 523, 524 and 525 schematically represent five alert windows which were determined by the window position determining procedure of Figs. 13A-13C for the first five contiguous cycle length categories selected out of the twelve cycle length categories of the non-limiting example disclosed hereinabove. It is noted that, for the sake of clarity of illustration, only these five selected alert windows are shown in the graph of Fig. 20 and the remaining other seven alert windows are not shown. It is also noted that, for the sake of clarity of illustration, the starting and ending points of the five alert windows represented by the horizontal lines 521, 522, 523, 524 and 525 are given in arbitrary time units from the time of detection of the RV event 11 and not in bin numbers (as they are stored in the array **WINDOW(CL,EV,ETC)** disclosed hereinabove). Thus, for example, the

alert window represented by the line 523 begins at the time represented by the projection of the beginning point **B3** of the line 523 on the horizontal time axis and ends at the time represented by the projection of the ending point **E3** of the line 523 on the horizontal time axis. Similarly, the alert windows represented by the lines 521, 522, 524 and 525 have beginning points **B1**, **B2**, **B4** and **B5** and ending points **E1**, **E2**, **E4** and **E5**, respectively.

The points **P1**, **P2**, **P3**, **P4** and **P5** represent the mid points of the cycle length categories used to determine the alert windows represented by the lines 521, 522, 523, 524 and 525, respectively. For example, the midpoint of a cycle length category (not shown in Fig. 20) including beat cycles from 550 to 650 millisecond long will be at 600 milliseconds on the vertical axis (point not shown). It is noted that, the graph of Fig. 20 is given by way of a schematic explanatory example only and does not represent actual experimentally derived values.

In accordance with one preferred embodiment of the present invention, the real time determination of the alert window for each beat cycle uses a piecewise linear approximation method. In the graph of Fig. 20 all the beginning points and ending points of all the determined alert windows (of which only the alert windows represented by the lines 521, 522, 523, 524 and 525 are illustrated) are connected by lines. For example, the beginning points **B1** and **B2** are connected by the dashed line 528, the beginning points **B2** and **B3** are connected by the dashed line 529 the beginning points **B3** and **B4** are connected by the dashed line 530, the beginning points **B4** and **B5** are connected by the dashed line 532. Similarly, the ending points **E1** and **E2** are connected by the dashed line 534, the ending points **E2** and **E3** are connected by the dashed line 535, the ending points **E3** and **E4** are connected by the dashed line 536, the ending points **E4** and **E5** are connected by the dashed line 538 . The slope of each of the lines 528, 529, 530, 532,534,535, 536 and 538 may be computed from the known values of the beginning points **B1**,**B2**, **B3**, **B4** and **B5**, and the ending points **E1**, **E2**, **E3**, **E4** and **E5**. When it is desired to compute the approximated beginning point **PB** and the approximated ending point **PE** of an alert window for a detected event having a measured interval

value represented by the point **PX** which lies on the vertical cycle length axis between the cycle length category midpoints **P4** and **P5**, the piecewise linear approximation is used by computing these values from equations 1 and 2 :

$$PB = B4 + (PX - P4)*(SLOPE\text{-}532) \quad (1)$$

$$PE = E4 + (PX - P4)*(SLOPE\text{-}538) \quad (2)$$

wherein **(SLOPE-532)** is the computed value of the slope of the line 532 and **(SLOPE-538)** is the computed value of the slope of the line 538. It is noted that the slopes of the lines 532 and 538 may or may not be identical and their values depend on the particular values of the points **B4** and **E4**, and **B5** and **E5** of the computed alert windows represented by the lines 524 and 525, respectively. Similarly, The values of the slopes of the lines 528 and 534, 529 and 535, and 530 and 524 depend on the particular determined values of the beginning and ending points of the corresponding computed alert windows represented by the lines 521, 522, 523, 524 and 525.

Preferably, as disclosed for the R-R interval represented by the point **PX**, the procedure for linear piecewise approximation uses the beginning and ending points of the line representing the alert window having an associated midpoint which has an equal or lower value than the value of the R-R interval and the slopes of the lines connecting the beginning and ending points of this line with the beginning and ending points of the line representing the alert window directly below it in the graph. However, if the R-R interval has a value smaller than the value of the point P1 on the vertical axis, the computation procedure uses the slopes of the lines 528 and 534. If the value of the R-R interval is equal to or larger than the value of the midpoint (not shown in Fig. 20) of the last cycle length category, the procedure uses for the computation the beginning and ending points of the last alert window (not shown in Fig. 20) and the slopes of the lines connecting the beginning point and ending point of the last alert

window with the corresponding beginning point and ending point of the alert window (not shown) which lies above the last alert window in the graph of Fig. 20

It is noted that, while the cycle length categories who's midpoints **P1**, **P2**, **P3**, **P4** and **P5** are shown in Fig. 20 do not span identical time ranges, other embodiments of the present invention may be implemented in which some or all of the cycle length categories span identical time ranges.

It is further noted that, for the non-limiting particular example used in describing the invention, for each acquired data set which is analyzed one may generate four different graphs, corresponding to the four possible combinations of the two variables **EV** and **ETC**. These combinations are **EV=SENSE, ETC=OFF**; **EV=SENSE, ETC=ON** ; **EV=PACE, ETC=OFF** ; and **EV=PACE, ETC=ON**. Each of these four graphs (not shown) includes twelve alert windows determined for the corresponding twelve cycle length categories of the non-limiting example of the invention disclosed hereinabove. Therefore, if one uses the non-limiting example using 12 cycle length categories disclosed hereinabove, the set of approximation parameters which is determined includes for each of the four possible combinations of **EV** and **ETC** 22 slope values, 12 beginning points and 12 ending points. Thus, the full set of approximation parameters includes 88 slope values, 48 beginning points and 48 ending points. However, if another number of cycle length categories is used in data acquisition, the number of approximation parameters will vary accordingly.

The full set of the approximation parameters is telemetrically or non-telemetrically programmed into the memory unit (not shown) of the implantable ETC device 19 of Fig. 3A or into the memory unit 44 of the devices 21 or 24 (Figs. 3A and 4, respectively) and is used in the operation of the devices 19, 21 and 24 for real-time computing of the approximation of the alert window beginning and ending time points for the various cycle lengths of detected beats under paced and sensed beat conditions in the absence and presence of the delivery of ETC signals.

Reference is now made to Fig. 21 which is a schematic flow control diagram illustrating the steps of an exemplary procedure for determining the real

time window approximation parameters of Fig. 19, in accordance with one preferred embodiment of the present invention. The procedure starts by computing the approximation parameters for all the possible combinations of the parameters **EV** and **ETC** from the data stored in the array **WINDOW(CL,EV,ETC)** and from the known bin size (step 600). The possible combinations are **EV=SENSE** and **ETC=OFF**; **EV=SENSE** and **ETC=ON** ; **EV=PACE** and **ETC=OFF** ; **EV=PACE** and **ETC=ON**. The approximation parameters include the beginning time points and ending time points for each of the alert windows determined for each cycle length category in each of the above possible parameter combinations. The approximation parameters also include the slopes of each of the lines connecting the beginning points (as disclosed hereinabove and illustrated in Fig. 20) and the slopes of each of the lines connecting the ending points (as disclosed hereinabove and illustrated in Fig. 20) for each of the above possible parameter combinations. The procedure then stores the full set of the approximation parameters in an array or LUT (step 602).

The procedure then determines the maximal sensitivity level values for each of the four combinations of the parameters **EV** and **ETC** and stores the resulting four maximal sensitivity level values in an array **SL_MAX (EV,ETC)** (step 604). The determination of the values of the maximal sensitivity depends on the specific detection method which is used for detecting the LV events and may be performed in any suitable method known in the art. For example, in the above disclosed case where a single positive threshold crossing method is used, one possible way to determines the maximal sensitivity level values is to sort each of the four groups **SENS(SENSE,CL,OFF)**, **SENS(SENSE,CL,ON)**, **SENS(PACE,CL,OFF)** and **SENS(PACE,CL,ON)** of sensitivity level values stored in the array **SENS(EV, CL,ETC)** (see Fig. 12) in ascending order and storing the last value in each of the sorted groups in the appropriate positions in the array **SL_MAX(EV,ETC)**. The sensitivity level value group **SENS(SENSE,CL,OFF)** includes the sensitivity levels determined for all the data histograms acquired for the parameter combination **EV=SENSE** and **ETC =OFF** (no pacing and no ETC signal delivery). The sensitivity level value group

**SENS(SENSE,CL,ON)** includes the sensitivity levels determined for all the data histograms acquired for the parameter combination **EV=SENSE** and **ETC =ON** (no pacing and with ETC signal delivery). The sensitivity level value group **SENS(PACE,CL,OFF)** includes the sensitivity levels determined for all the data histograms acquired for the parameter combination **EV=PACE** and **ETC =OFF** (with pacing and no ETC signal delivery). The sensitivity level value group **SENS(PACE,CL,ON)** includes the sensitivity levels determined for all the data histograms acquired for the parameter combination **EV=PACE** and **ETC =ON** (with pacing and with ETC signal delivery).

In the non-limiting example disclosed hereinabove each of the groups to be sorted **SENS(SENSE,CL,OFF)**, **SENS(SENSE,CL,ON)**, **SENS(PACE,CL,OFF)** and **SENS(PACE,CL,ON)** includes 12 values of determined sensitivity levels. It will be appreciated by those skilled in the art that many other ways of determining the maximal sensitivity levels may be used, depending on the type of event detection method which is used. Thus, the method of determining the maximal sensitivity levels for each of the above four groups **SENS(SENSE,CL,OFF)**, **SENS(SENSE,CL,ON)**, **SENS(PACE,CL,OFF)** and **SENS(PACE,CL,ON)**, may be adapted to the type of event detection method which is used. The array **SL_MAX(EV,ETC)** is also telemetrically or non-telemetrically programmed into the memory unit (not shown) of the implantable ETC device 19 of Fig. 3A or into the memory unit 44 of the devices 21 or 24 (Figs. 3A and 4, respectively) and is used in the operation of the devices 19, 21 and 24 for real-time setting of the detection sensitivity level of the devices 19, 21 and 24 as is disclosed in detail hereinafter.

Finally, the procedure returns control to the common window position parameters determining procedure of Fig. 19 ( step 606 ).

The approximation parameter array or LUT, is used for programming of the implantable ETC device 19 of Fig. 3A or the devices 21 or 24 (Figs. 3A and 4, respectively) as disclosed hereinabove. After programming, the approximation parameters are used for real-time determination of the approximated alert window beginning and ending points as disclosed in detail hereinabove and illustrated in Fig. 20. For instance, in the case of the

non-limiting example disclosed hereinabove which includes 12 cycle length categories in each of the four possible combinations of the parameters **EV** and **ETC**, the stored array or LUT includes 88 slope values, 48 beginning points and 48 ending points.

Reference is now made to Fig. 22 which is a schematic control flow diagram illustrating the steps of a method for real time determination of the beginning and ending time points of an alert window and of the detection parameters in an ETC device having pacing capabilities, in accordance with a preferred embodiment of the present invention. The program implementing the method of Fig. 22 is operative in the devices 19, 21 and 24 after they have been programmed with the appropriate data. The data includes the value of the flag **DFLAG**, the array or LUT of approximation parameters as disclosed hereinabove and the array of maximal sensitivity level values **SL_MAX (EV,ETC)**. The program starts by getting the current value of the parameter **ETC** (step 650). During the real-time operation of the program, the current value of the parameter **ETC** is continuously updated in real-time by the procedure disclosed hereinabove and illustrated in Fig. 10. The program then checks if the pacemaker circuitry sensed an event (step 652). If the pacemaker sensed an event, the program checks if a PVC was detected (step 654). If a PVC was detected, the program does not allow the delivery of an ETC signal for the current beat and returns control to step 650. If a PVC was not detected, the program updates the value of the parameter **EV** by setting it's value to **EV**=SENSE (step 656), and checks the value of the flag **DFLAG** (step 658).

If in step 652, the pacemaker has not sensed, the program checks if the pacemaker has paced (step 660). If the pacemaker paced, the program updates the value of the parameter **EV** by setting it's value to **EV**=PACE (step 662), and transfers control to step 658 for checking the value of the flag **DFLAG**. If the pacemaker did not pace control is returned to step 652.

In step 658, if **DFLAG**=1, the program gets the current measured value of the R-R interval from the pacemaker circuitry (step 664), selects the appropriate approximation parameters for the current R-R interval as disclosed in detail hereinabove (step 666) and computes the current values of the alert window

parameters **WINBEG** representing the approximated beginning time of the alert window and **WINEND** representing the approximated ending time of the alert window by using the equations 1 and 2 as disclosed in detail hereinabove and illustrated in Fig. 20 ( step 668).

For example, if the R-R interval is equivalent to the value represented by the point **PX** of Fig. 20, step 666 selects the value of the beginning point **B4** (Fig. 20), the ending point **E4** (Fig. 20) and the slopes of the lines 532 and 538 (Fig. 20) and in step 668 computes **PB** and **PE** from equations 1 and 2, respectively, and set **WINBEG=PB** and **WINEND=PE**.

The program then sets the current sensitivity level to be used by the detection circuitry by using the sensitivity level stored in the array **SL_MAX(EV,ETC)** in the array position defined by the current values of the parameters **EV** and **ETC** (step 670) and returns control to step 650.

In step 658, if the value of the flag **DFLAG** is not equal to 1, this indicates that a single pair of values for the alert window beginning time point and ending time points and a single common sensitivity value were selected as adequate for use with all R-R intervals measured in real-time irrespective of the cycle length category into which the measured R-R interval fits (as disclosed in detail in steps 502, 508, 510 and 512 of Fig. 19). The program then updates the values of the parameters **WINBEG** and **WINEND** by using the two values **MINBEG** and **MAXEND** stored in the array **TOT_WINDOW** (see Fig. 19) such that **WINBEG=MINBEG** and **WINEND=MAXEND** (step 672), sets the sensitivity level to the value stored in **SENS_LEVEL** (step 674) and returns control to step 650.

It will be appreciated by those skilled in the art that the preferred embodiment of the program for real-time determination of the alert window parameters and the detection sensitivity level disclosed hereinabove and illustrated in Fig. 22, is given by way of example only, and that many variations and modifications thereof are possible which are included within the scope of the present invention. For example, while the steps 666 and 668 of the method of Fig. 22 select the proper linear piecewise approximation parameters and computes the values of the alert widow beginning and ending time points

**WINBEG** and **WINEND** from the selected linear piecewise approximation parameters and the measured R-R interval, other methods (not shown) for computing **WINBEG** and **WINEND** may also be used based on other approximation methods known in the art such as, but not limited to, spline approximation methods, or the like. Additionally, in accordance with another preferred embodiment of the present invention, the steps the steps 666 and 668 of Fig. 22 may be replaced by steps (not shown) which do not perform an approximation computation but instead compute the beginning point and ending point of the alert window directly from the beginning bin number and the ending bin number of the array **WINDOW(EV,CL,ETC)** and from the known bin size ( the bin duration). In this preferred embodiment, the data in the LUT which is stored in the device includes the array **WINDOW(EV,CL,ETC),** the array **SL_MAX(EV,ETC)**, the value of the flag **DFLAG** and the bin size (in time units). As disclosed hereinabove, the latter embodiment may be used in cases where the data acquisition was performed using a large number of cycle length categories which may obviate the need for performing the approximation.

It is noted that, while the above disclosed methods and procedures are adapted for devices which include pacing circuitry, such as the implantable device 21 of Fig. 3A, the analyzing unit 64 of the system 60 of Fig. 5 and the like, the methods of the present invention may also be adapted with some modifications for use with devices having no cardiac pacing capability, such as the device 24 of Fig.4, the analyzing unit 74 of the system 70 of Fig. 6 and the like.

Reference is now made to Figs. 23A-23B which are schematic flow control diagrams illustrating the steps of a method for acquiring time histogram data sets under various cardiac conditions in the absence of artificial cardiac pacing and for determining one or more sets of alert window parameters or approximation parameters and one or more detection parameter sets from the histogram data, in accordance with a preferred embodiment of the present invention.

The method illustrated in Figs. 23A-23B is a modified version of the more general method disclosed hereinabove and illustrated in Figs. 8B-8C. The

difference between the two procedures is that in the method of Figs. 23A-23B there is no pacing during the data acquisition time period.

The data collection program embedded within the pacemaker/ETC device 24 of Fig. 4 or the analyzing unit 74 of Fig. 6 starts by checking whether the user or operator has terminated the collection of data (step 690). The user (typically the cardiologist) may terminate data collection by a suitable command which is transmitted telemetrically to the pacemaker/ETC device 24, or input manually to the analyzing unit 74 of the system 70 through one of the user interface device(s) 69. Typically, the command may set a suitable flag or change the value of a variable which is checked by the program. However, other suitable methods for terminating data collection may be used. If the user did terminate data collection the data collection program ends (step 692). If the user did not terminate data collection, the program gets the current sensitivity level value **SL** (step 694). The sensitivity level variable **SL** may be an integer variable which can take any integer value selected from a group of integer numbers, each representing a particular sensitivity value available for use in the pacemaker/ETC device 24 or the analyzing unit 74. For example, if the event detection sensitivity is determined by the crossing of a single voltage threshold and the pacemaker/ETC device can have 8 different sensitivity levels, **SL** may be any integer in the range 1-8.

The data collection program checks whether the device 24 (or the analyzing unit 74 ) sensed an event in the RV chamber (step 696). This is performed by the appropriate sensing unit of the sensing units 38 which is operatively associated with the sensing electrode (not shown) of the implantable leads 22 which is positioned in the RV. If the device sensed an RV event, the data collection program sets the value of the logical parameter to **EV**=SENSE to indicate a sensed beat cycle (step 699) and checks whether a premature ventricular contraction (PVC) was detected (step 700). The detection of a PVC is performed by the ETC device 24 or by the pacing program operating the processing unit 61 of the analyzing unit 74.

It is noted that, while the device 24 and the analyzing unit 74 do not include pacing circuitry for pacing the heart, they do contain suitable circuitry

(not shown in detail) which is capable of detecting PVCs. A PVC may be detected using the signals sensed in the RV. As is known in the art, PVC's may be identified by detecting two consecutive ventricular events without an atrial event therebetween. For example, the PVC detection methods used in pacemakers operating in a DDD mode are suitable for use in the data collection method of the present invention.

However, other methods suitable for PVC detection may be used. PVC detection methods are well known in the art, are not the subject matter of the present invention and will therefore not be discussed in detail hereinafter.

If a PVC was detected the data collection program returns control to step 690 for avoiding collection of data for the current beat cycle. If a PVC was not detected, the data collection program gets the value of the variable **ETC** (step 701). The variable **ETC** is a logical variable which can have the values "ON" and "OFF". When **ETC**=OFF the histogram represents data considered to be collected under conditions in which there was no practically substantial influence of the delivery of ETC signals on the cardiac conduction velocity. When **ETC**=ON the histogram represents data considered to be collected under conditions in which the delivery of ETC signals has substantial influence of on the cardiac conduction velocity. The detailed procedure of setting the value of the variable **ETC** and the criteria used to set the value of the variable **ETC** are disclosed in detail hereinabove and illustrated in Fig 10. The remaining steps of the data acquisition program of Figs. 23A-23B are similar to the equivalent steps of the data acquisition program of Figs. 8B-8C. Steps 701, 702, 704, 705, 706, 708, 710, 712, 714, 716, 718 and 720 of Figs. 23A-23B are similar to steps 101, 102, 104, 105, 106, 108, 110, 112, 114, 116, 118 and 120, respectively, of Figs. 8B-8C, except that the data histograms **HIST(EV,CL,SL,ETC)** of the steps of Figs. 23A-23B represent a degenerate set of the data histograms **HIST(EV,CL,SL,ETC)** of Figs. 8B-8C since the value of the parameter **EV**, as set by step 699 of the method of Fig. 23A, can only be **EV** =SENSE because the device 24 and the analyzing unit 74 have no pacing capability. Thus, the total number of the data histograms acquired by the data acquisition method of

Figs. 23A-23B is half of the total number of the data histograms acquired by the data acquisition method of Figs. 8B-8C.

It is noted that in step 712 of Fig. 23B, if **TIME≥MAXDELAY,** control is returned to step 690. In step 720 of Fig. 23B, if **TIME>MAXDELAY**, control is returned to step 690.

It is further noted that, when the data acquisition is performed by the device 24 of Fig. 4 or by the analyzing unit 74 of Fig. 6, using the data acquisition program illustrated in Figs. 23A-23B, the program for determining the parameters of the alert window in real-time must also be modified since no pacing is performed by the device 24 or the analyzing unit 74.

Reference is now made to Fig. 24 which is a schematic control flow diagram illustrating the steps of a method for real time determination of the beginning and ending time points of an alert window and of the detection parameters in a non-pacing ETC device, in accordance with another preferred embodiment of the present invention.

The program implementing the method of Fig. 24 is operative in the device 24 of Fig. 3A or in the analyzing unit 74 of the system 70 of Fig. 6 after they have been programmed with the appropriate data. The data includes the value of the flag **DFLAG**, the array or LUT of approximation parameters as disclosed hereinabove and the array of maximal sensitivity level values **SL_MAX(EV,ETC)**.

It is noted that while the device 24 and the analyzing unit 74 do not have pacing capability, they include all the necessary circuitry and embedded programs for sensing and detecting events in one or more cardiac chambers as is known in the art and they are capable of determining and storing the R-R interval of the current beat as is known in the art. If the device 24 is used, the current value of the R-R interval is stored in the memory unit 44. If the analyzing unit 74 is used, the current value of the R-R interval is stored in the memory unit 66.

The program starts by getting the current value of the parameter **ETC** (step 850). During the real-time operation of the program, the current value of the parameter **ETC** is continuously updated in real-time by the procedure

disclosed hereinabove and illustrated in Fig. 10. The program then checks if the detection circuitry sensed an event in the right ventricle chamber (step 852). When the program is embedded in the device 24 of Fig. 4, the sensing is performed by the appropriate sensing unit of the sensing units 38 which is associated with the sensing electrode positioned in the right ventricle such as the electrode or electrode pair 4A (Fig. 1). When the program is embedded in the analyzing unit 74 of Fig. 6, the sensing is performed by the circuitry of the front end 62 which is associated with the sensing electrode positioned in the right ventricle such as the electrode or electrode pair 4A (Fig. 1). If an event was sensed in the right ventricle chamber, the program checks if a PVC was detected (step 854). If a PVC was detected, the program does not allow the delivery of an ETC signal for the current beat and returns control to step 850. If a PVC was not detected, the program updates the value of the parameter **EV** by setting it's value to **EV=SENSE** (step 856), and checks the value of the flag **DFLAG** (step 858).

In step 858, if **DFLAG=1**, the program gets the current measured value of the R-R interval from the memory unit 44 of the device 24 or from the memory unit 66 of the analyzing unit 74 (step 864), selects the appropriate approximation parameters for the current R-R interval as disclosed in detail hereinabove (step 866) for Fig. 22 and computes the current values of the alert window parameters **WINBEG** representing the approximated beginning time of the alert window and **WINEND** representing the approximated ending time of the alert window by using the equations 1 and 2 as disclosed in detail hereinabove and illustrated in Fig. 20 ( step 868).

The program then sets the current sensitivity level to be used by the detection circuitry by using the sensitivity level stored in the array **SL_MAX(EV,ETC)** in the array position defined by the current value of the parameter **ETC** (step 870) and returns control to step 650. It is noted that the array **SL_MAX(EV,ETC)** as determined by the data acquisition program of Figs. 23A-23B is a degenerate form of the array **SL_MAX(EV,ETC)** determined by the data acquisition program of Figs. 8B-8C since the parameter **EV** can have only the value **EV=SENSE**, therefore the degenerate array **SL_MAX(EV,ETC)**

includes only two valid sensitivity levels for the cases in which **ETC**=ON and **ETC**=OFF.

In step 858, if the value of the flag **DFLAG** is not equal to 1, this indicates that a single pair of values for the alert window beginning time point and ending time points and a single common sensitivity value were selected as adequate for use with all R-R intervals measured in real-time irrespective of the cycle length category into which the measured R-R interval fits (as disclosed in detail in steps 502, 508, 510 and 512 of Fig. 19). The program then updates the values of the parameters **WINBEG** and **WINEND** by using the two values **MINBEG** and **MAXEND** stored in the array **TOT_WINDOW** (see Fig. 19) such that **WINBEG=MINBEG** and **WINEND=MAXEND** (step 872), sets the sensitivity level to the value stored in **SENS_LEVEL** (step 874) and returns control to step 850.

It is noted that, the program of Fig. 24 may be modified to use various different approximation methods such as a spline approximation method or other suitable approximation methods for computing the approximated alert window beginning and ending time points, as disclosed for the program of Fig. 22 hereinabove. Additionally, in accordance with another preferred embodiment of the present invention, the steps the steps 866 and 868 of Fig. 24 may be replaced by steps (not shown) which do not perform an approximation computation but instead compute the beginning point and ending point of the alert window directly from the beginning bin number and the ending bin number of the array **WINDOW(EV,CL,ETC)** and from the known bin size (the bin duration). In this preferred embodiment, the data in the LUT which is stored in the device includes the array **WINDOW(EV,CL,ETC)**, the array **SL_MAX(EV,ETC)**, the value of the flag **DFLAG** and the bin size (in time units). As disclosed hereinabove, this embodiment may be used in cases where the data acquisition was performed by the program of Figs. 8B-8C using a large number of cycle length categories which may obviate the need for performing the approximation.

It is further noted that all the methods and procedures disclosed hereinabove are adapted for use with devices having detection circuitry which is

capable of fast switching of the detection sensitivity in real-time. This means that at least one of the sensing units 38 of the devices 21 and 24 is capable of controllably switching from one sensitivity level to another sensitivity level within a time period which is short enough to implement sensitivity level changes from one heart beat to the next heart beat. Similarly, the front end 62 of the analyzing units 64 and 74 will also be capable of controllable fast switching between different sensitivity levels. For example, the sensitivity level may be controllably switched by controllably changing the threshold level of a comparator circuit (not shown). However, other suitable methods may be used for sensitivity changing. The design and implementation of such fast circuits for changing detection sensitivity levels is well known in the art, is not the subject matter of the present invention and is therefore not disclosed in detail herein. Moreover, even if the circuitry of a device used for patient data collection is not fast enough to affect a sensitivity level change on a beat by beat basis, the full set of histogram data may still be collected by acquiring data at a first sensitivity level from a first group of beats, changing the sensitivity level, acquiring data from a second group of beats and so forth until enough data has been acquired for all sensitivity levels.

It is still further noted that, while in the programs disclosed hereinabove and illustrated in Figs. 22 and 24 the various determined approximation parameters are stored in an LUT or array, the various determined sensitivity levels are stored in an array **SL_MAX(EV,ETC)** and/or a variable **SENS_LEVEL**, and **DFLAG** may be stored in the LUT or separately, the way of storing the approximation parameters, the sensitivity levels and the value of **DFLAG** is not critical to the invention and many different ways of organizing and storing this information may be implemented as is well known in the art.

It is yet further noted that, while the present invention is disclosed as adapted for use in the ETC devices and in ETC/pacemaker devices disclosed hereinabove, the methods of the present invention may also be adapted for use in devices having additional capabilities. For example, in accordance with another preferred embodiment of the present invention, devices may be implemented which include in addition to the pacing capabilities and the ETC

signal delivering capabilities, the capability to deliver defibrillation pulses to the heart as is well known in the art.

Furthermore, while the programs and procedures disclosed hereinabove are adapted for use with an exemplary embodiment of the present invention which uses the R-R interval computed from events sensed in or about the right ventricle, other preferred embodiments of the present invention may be adapted for using an A-A interval which is the computed time interval between consecutive detected atrial events which are locally sensed in or about the right atrium. The electrode configurations for such a preferred embodiment are disclosed in detail in the above referenced International Application No. PCT/IL00/00126 Titled "APPARATUS AND METHOD FOR TIMING THE DELIVERY OF NON-EXCITATORY ETC SIGNALS TO A HEART".

Further yet, for each beat cycle, after the beginning and ending time points of the dynamic alert window and the detection sensitivity level have been determined as disclosed hereinabove, if an ETC non-excitatory signal is delivered to the heart, the delivery may be performed as disclosed in detail hereinabove (Fig. 2) or as disclosed in the above referenced International Application No. PCT/IL00/00126 Titled "APPARATUS AND METHOD FOR TIMING THE DELIVERY OF NON-EXCITATORY ETC SIGNALS TO A HEART".

In accordance with still another preferred embodiment of the present invention, the ETC device and the ETC/pacemaker device may also have fencing capabilities as disclosed in detail in PCT Application, International Publication Number WO 98/10830, titled "FENCING OF CARDIAC MUSCLES" to Ben Haim et al.

It is noted that throughout the present application the term "real-time" is used broadly to imply on-line performance of determinations, computations and approximations which are performed on the fly by the devices of the present invention for each cardiac beat cycle.

It is further noted that in the preferred embodiments of the invention disclosed hereinabove and illustrated in Figs. 22 and 24 the value of the R-R interval which is used for determining the alert window beginning and ending

time points is the currently measured "instantaneous" time interval between the detection of an RV event in the previous heart beat and the detection of an RV event in the current heart beat. However, due to the natural fluctuation of the R-R intervals it may be desired to use an average R-R interval for the real time computation of the alert window beginning and ending time points. Thus, in accordance with another preferred embodiment of the present invention, the procedures of Figs. 22 and 24 may compute the current value of an average R-R interval (the detailed steps of such a computation of an average interval are well known in the art and are therefore not shown in Figs. 22 and 24) and use it for the real-time computation of the alert window beginning and ending time points. For example, the programs of Figs. 22 and 24 may store the R-R-intervals of the last K consecutive heart beats in a the memory 44 or 66 and compute the average R-R interval by summing these K R-R intervals and dividing the sum by K for each heart beat. In the next heart beat, the value of the currently measured R-R interval is added to the beginning of the list of K values, the earliest of the stored R-R interval values is removed from the list and the average is computed again. This may be implemented using a first in first out (FIFO) buffer or by any other suitable method for computing a dynamic average known in the art. When such an averaged R-R interval is used for computing the alert window beginning and ending time points, the number of stored R-R interval values K is preferably a small number in the range of 2 -5 to reduce the possible effect of masking or attenuating abrupt changes in the R-R interval due to the averaging.

Since spurious detection in the RV of signals which are not true RV events may introduce an error in the calculation of such an average R-R interval, it may be desired to use the median of the R-R interval values instead of using their average. In such preferred embodiments which use a computed median, the median value may preferably be computed from a number of stored R-R interval in the range of approximately 5-8 stored R-R interval to reduce errors due to PVCs and the like.

While the invention has been described with respect to a limited number of embodiments, it will be appreciated by the person skilled in the art that many variations, modifications and other applications of the invention may be made.

CLAIMS

1. A method for obtaining from a patient's heart data useful for on-line determining of the parameters of an alert time window in an excitable tissue control device, the method comprising the steps of:

Applying electrodes to a first cardiac site and a second cardiac site of said patient and electrically connecting said electrodes to a data collecting device;

Operating said device under a plurality of different cardiac conditions to obtain a plurality of different histogram data sets, each histogram data set of said plurality of histogram data sets represents a cumulative time distribution histogram of cardiac depolarization events detected at said second cardiac site in a plurality of cardiac beats, each histogram data set of said plurality of histogram data sets is associated with a plurality of histogram parameters, said histogram parameters have values indicative of the cardiac conditions common to said plurality of cardiac beats used to obtain said histogram data set, said histogram parameters include a sensitivity level parameter having a value indicative of the detection sensitivity level used for detecting said cardiac depolarization events of said plurality of cardiac beats at said second cardiac site;

Processing said plurality of histogram data sets to compute a set of data usable for on-line determination of the parameters of said alert time window.

2. The method according to claim 1 wherein said step of operating comprises the steps of:

Setting a selected value for said detection sensitivity level parameter, by selecting a value from a plurality of values indicative of the plurality of detection sensitivity levels operatively available in said data collection device and

adjusting said data collection device to use the detection sensitivity level indicated by said selected value;

Updating the values of said histogram parameters in accordance with the current cardiac conditions;

selecting a histogram data set to be updated based on the current values of said plurality of histogram parameters;

triggering a data collection time interval having a first duration, said data collection time interval comprises a plurality of contiguous time bins having a second duration smaller than said first duration, each of said time bins is associated with a single data element of a plurality of data elements included in said histogram data set, the value stored in a data element of said plurality of data elements represents the number of depolarization events detected in a plurality of beats at said second cardiac site within said second duration of the time bin associated with said data element;

using the times of detection of depolarization events at said second cardiac site within the duration of said data collection time interval to update the number of detected depolarization events recorded in appropriate data elements of said histogram data set; and

repeating said steps of setting, updating, selecting ,triggering and using for a desired number of cardiac beats.

3. The method according to claim 1 wherein one of said plurality of histogram parameters is a cycle length category parameter, the value of said cycle length category parameter may be one of a plurality of preset values, each value of said plurality of preset values represents a predetermined range of beat to beat time intervals, and wherein the current value of said cycle length category represents a cycle length category having a range within which the current beat to beat time interval falls, wherein said current beat to beat time interval is defined as the time interval between the currently detected depolarization event at said first cardiac site and the depolarization event

detected at said first cardiac site in the cardiac beat preceding the current cardiac beat.

4. The method according to claim 3 wherein said first cardiac site is the right ventricle of said heart, said second cardiac site is the left ventricle of said heart and wherein said beat to beat time interval is the R-R interval computed from the time of detection of the right ventricular depolarization event of the current cardiac beat and the time of detection of the right ventricular depolarization event of the cardiac beat preceding said current cardiac beat.

5. The method according to claim 3 wherein said first cardiac site is the right atrium of said heart, said second cardiac site is the left ventricle of said heart and wherein said beat to beat time interval is the A-A interval computed from the time of detection of the right atrial depolarization event of the current cardiac beat and the time of detection of the right atrial depolarization event of the cardiac beat preceding said current cardiac beat.

6. The method according to claim 1 wherein one of said plurality of histogram parameters may have two possible different values, a first value representing a first cardiac condition in which any excitable tissue control signals which were applied to said heart prior to the current cardiac beat did not substantially change the conduction velocity of the depolarization wave through the myocardium of said heart and a second value different than said first value representing a second cardiac condition in which any excitable tissue control signals which were applied to said heart prior to the current cardiac beat did not substantially change the conduction velocity of the depolarization wave through the myocardium of said heart.

7. The method according to claim 1 wherein one of said plurality of histogram parameters may have a value equal to one of two possible different values, one value representing a third cardiac condition in which the current cardiac beat is evoked by the natural pacemaker of the heart and another value representing a fourth cardiac condition in which the current cardiac beat is

evoked by a pacing pulse delivered to the myocardium of said heart by said data collection device through one of said electrodes.

8. The method according to claim 7 wherein said triggering of said step of triggering a data collection time interval is initiated upon delivering by said data collection device of a pacing pulse to said heart through one of said electrodes.

9. The method according to claim 2 wherein said triggering of said step of triggering a data collection time interval is initiated upon detecting a depolarization event at said first cardiac site.

10. The method according to claim 2 wherein said selecting of said step of setting comprises randomly or pseudo-randomly selecting a value from said plurality of values indicative of the plurality of detection sensitivity levels operatively available in said data collection device.

11. The method according to claim 2 wherein said selecting of said step of setting comprises selecting a single optimized value from said plurality of values based on the determining by an operator of said data collection device of an optimal detection sensitivity level in a data collection session occurring prior to said step of setting.

12. The method according to claim 2 wherein said selecting of said step of setting comprises selecting a value from said plurality of values in accordance with a predetermined schedule for periodically changing the detection sensitivity level, wherein said schedule is arranged to result in sufficient data being recorded for each different value of detection sensitivity level during the period of time used for data acquisition in said patient.

13. The method according to claim 2 further including between said step of setting and said step of updating the step of delivering a pacing pulse to said heart.

14. The method according to claim 2 further including the step of delivering a non-excitatory ETC signal to said heart after said data collection time interval is terminated.

15. The method according to claim 1 wherein said step of operating further includes the step of pacing said heart thorough one of said electrodes.

16. The method according to claim 15 wherein said step of pacing includes changing the A-V delay used for said pacing to change the ratio of paced and non-paced beats.

17. The method according to claim 15 wherein said changing of said A-V delay is performed manually by the operator of said data collection device.

18. The method according to claim 15 wherein said changing of said A-V delay is performed automatically by said data collection device.

19. The method according to claim 1 wherein said data collecting device is implanted in said patient.

20. The method according to claim 1 wherein said plurality of different histogram data sets obtained in said step of operating is telemetrically transmitted to an analyzing unit external to the body of said patient prior to said step of processing.

21. The method according to claim 1 wherein said data collecting device connected to said electrodes is an analyzing unit disposed external to the body of said patient.

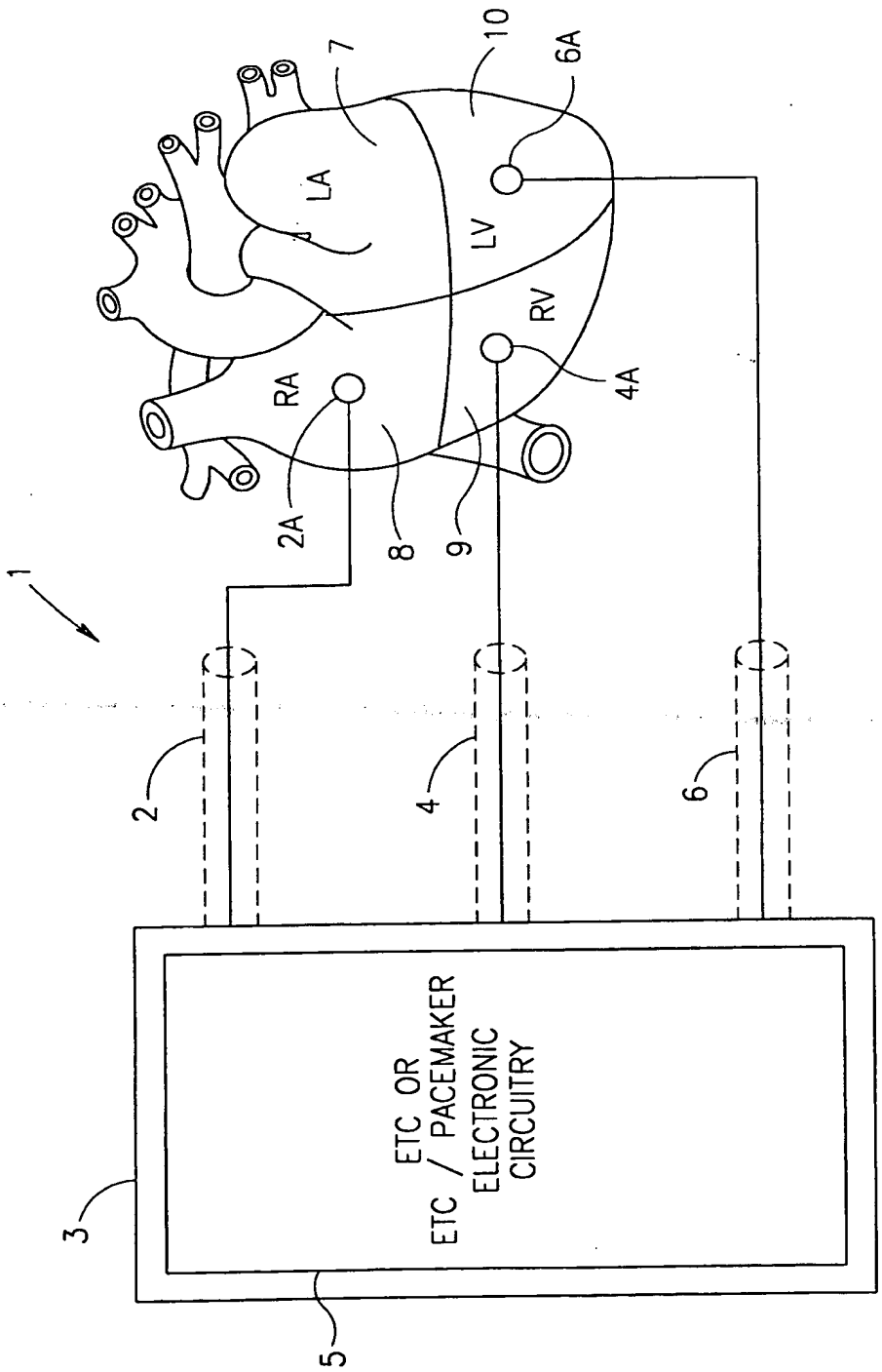

1
2
2A
3
4
4A
5
6
6A
7
8
9
10
LA
LV
RA
RV
ETC OR
ETC / PACEMAKER
ELECTRONIC
CIRCUITRY

FIG.1

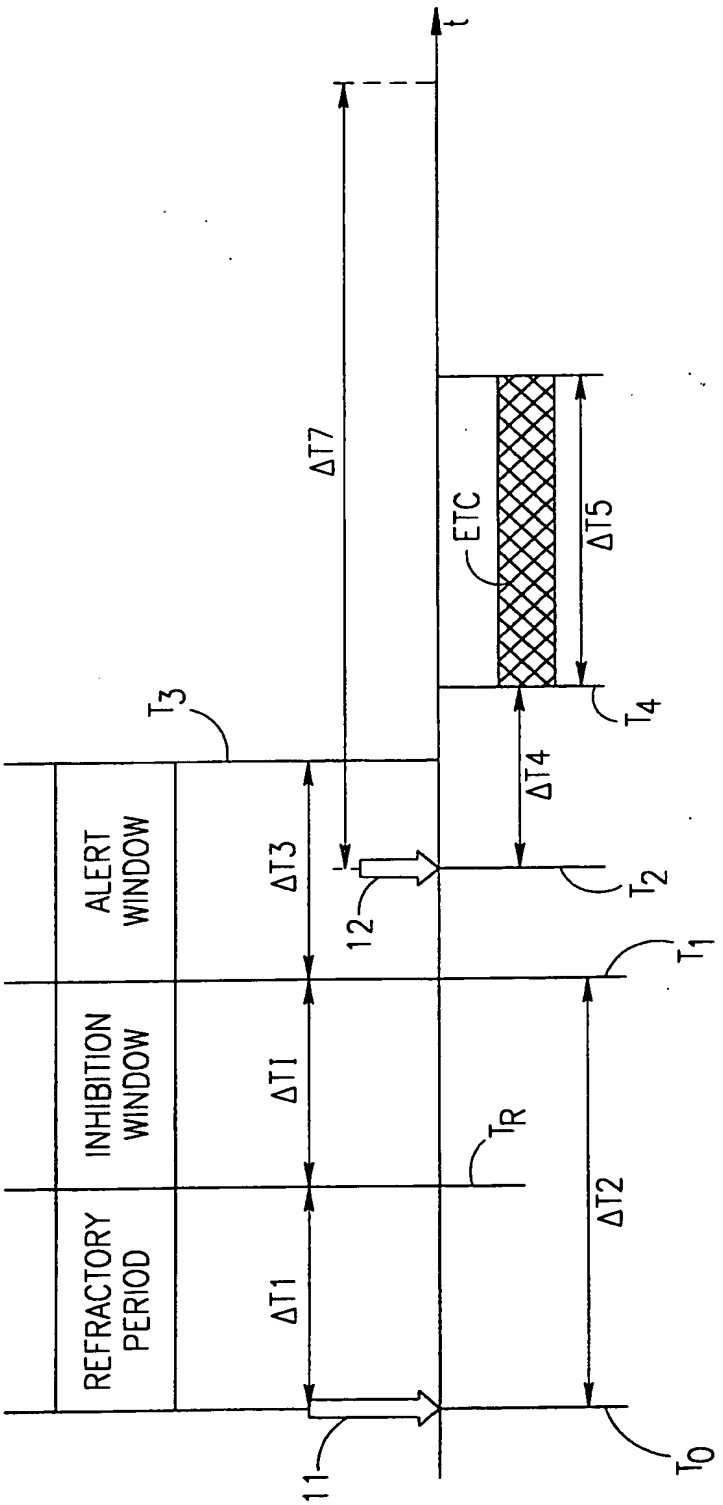

t
ΔT7
ETC
ΔT5
T3
T4
ΔT4
ALERT WINDOW
ΔT3
12
T2
T1
INHIBITION WINDOW
ΔT1
TR
ΔT2
REFRACTORY PERIOD
ΔT1
11
T0

FIG.2

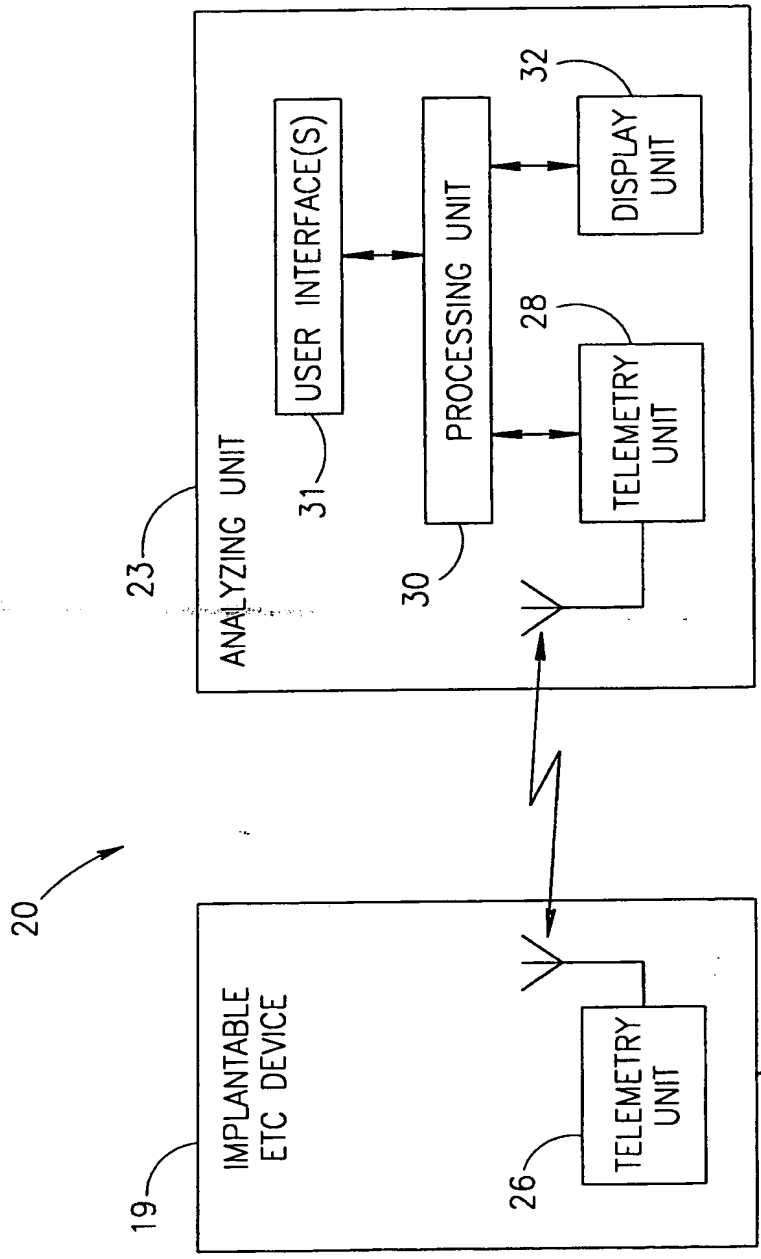

20
ANALYZING UNIT
23
USER INTERFACE(S)
31
PROCESSING UNIT
30
DISPLAY UNIT
32
TELEMETRY UNIT
28
IMPLANTABLE ETC DEVICE
19
TELEMETRY UNIT
26
IMPLANTABLE LEADS
22

FIG.3A

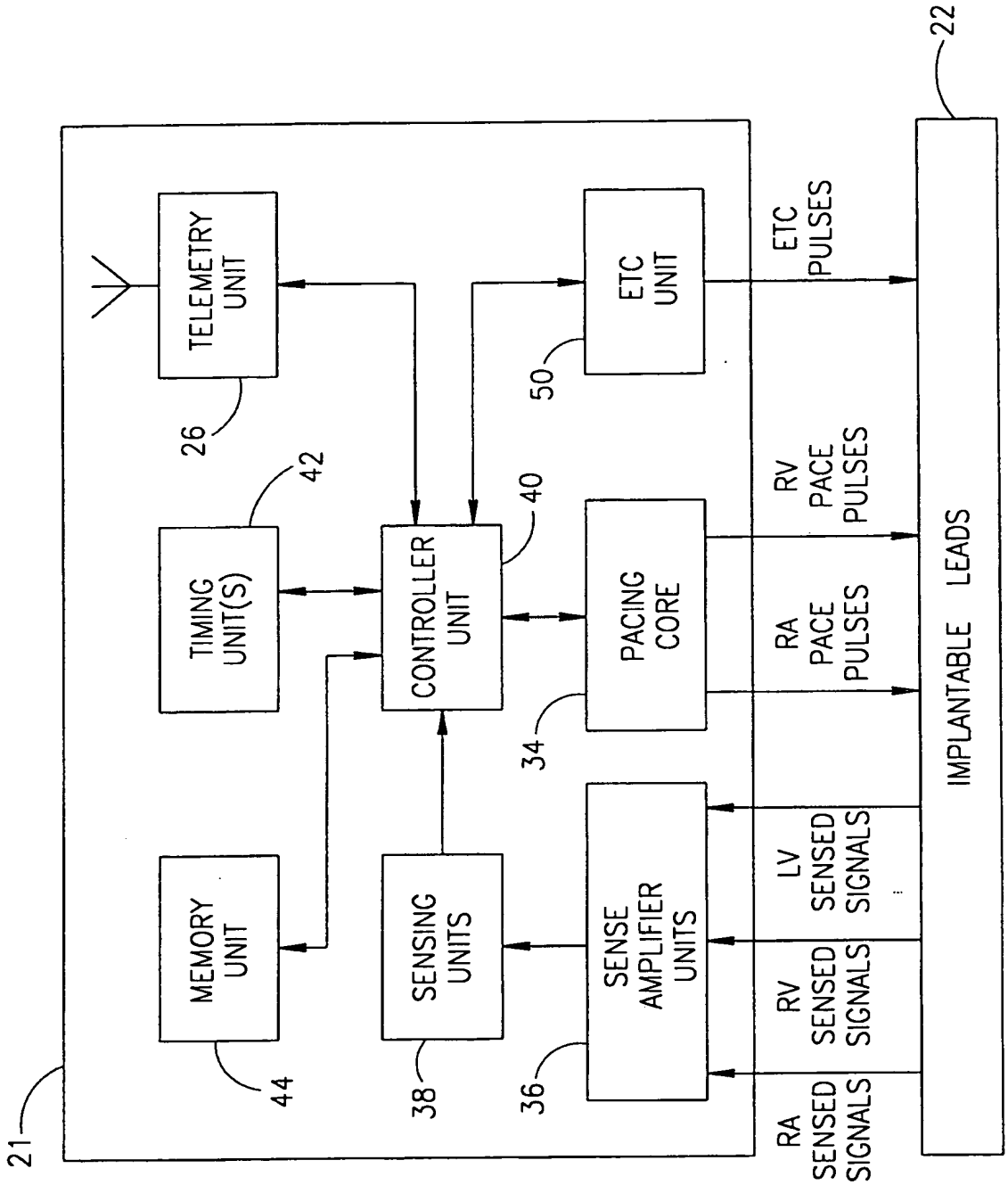

22
TELEMETRY UNIT
26
ETC UNIT
50
ETC PULSES
42
TIMING UNIT(S)
CONTROLLER UNIT
40
PACING CORE
RV PACE PULSES
RA PACE PULSES
34
IMPLANTABLE LEADS
MEMORY UNIT
44
SENSING UNITS
38
SENSE AMPLIFIER UNITS
36
LV SENSED SIGNALS
RV SENSED SIGNALS
RA SENSED SIGNALS
21

FIG.3B

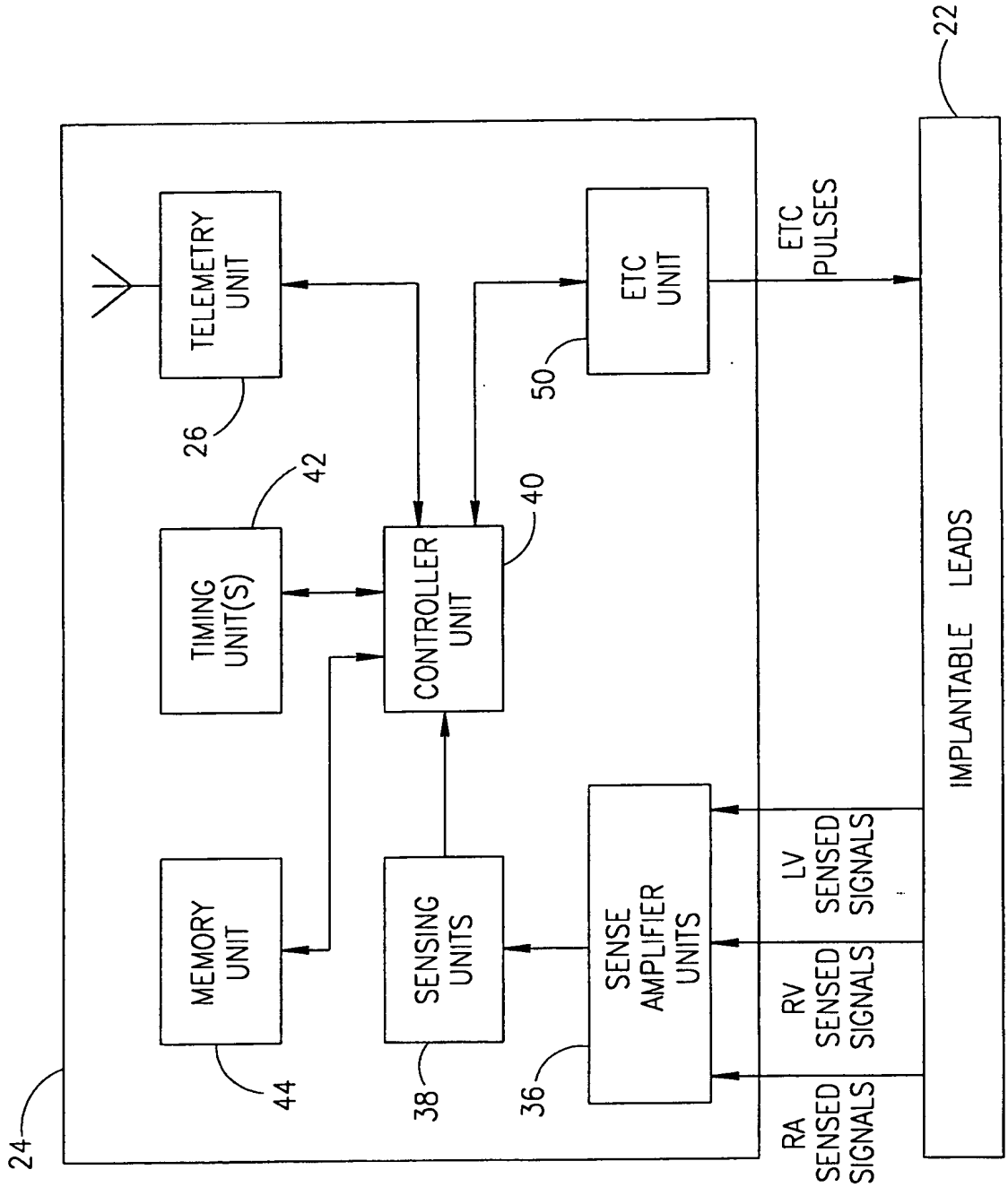

22
TELEMETRY UNIT
26
ETC UNIT
50
ETC PULSES
42
40
TIMING UNIT(S)
CONTROLLER UNIT
IMPLANTABLE LEADS
MEMORY UNIT
SENSING UNITS
SENSE AMPLIFIER UNITS
LV SENSED SIGNALS
RV SENSED SIGNALS
RA SENSED SIGNALS
24
44
38
36

FIG.4

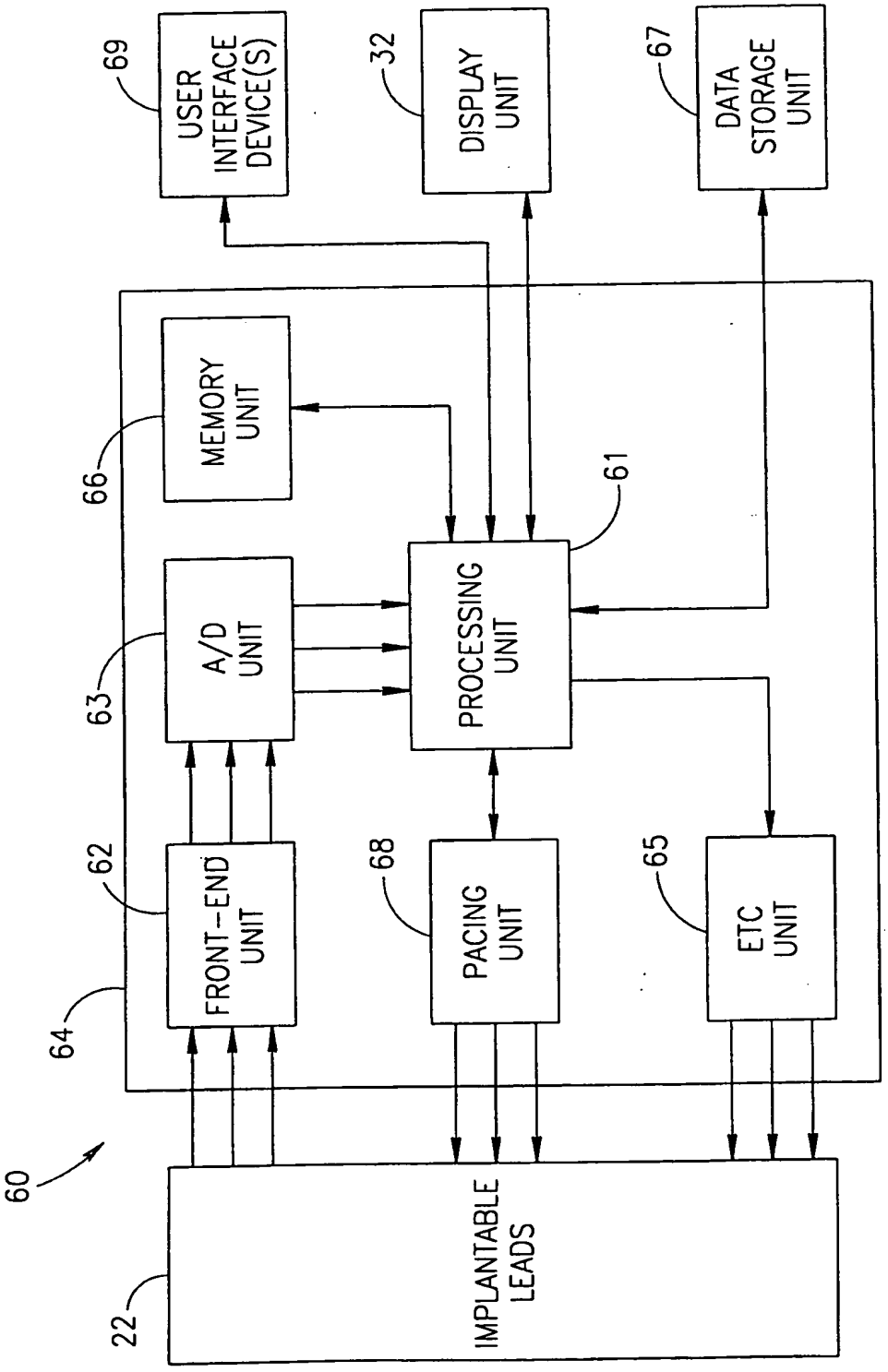

USER INTERFACE DEVICE(S)
69
DISPLAY UNIT
32
DATA STORAGE UNIT
67
MEMORY UNIT
66
61
A/D UNIT
63
PROCESSING UNIT
FRONT-END UNIT
62
PACING UNIT
68
ETC UNIT
65
64
60
IMPLANTABLE LEADS
22

FIG.5

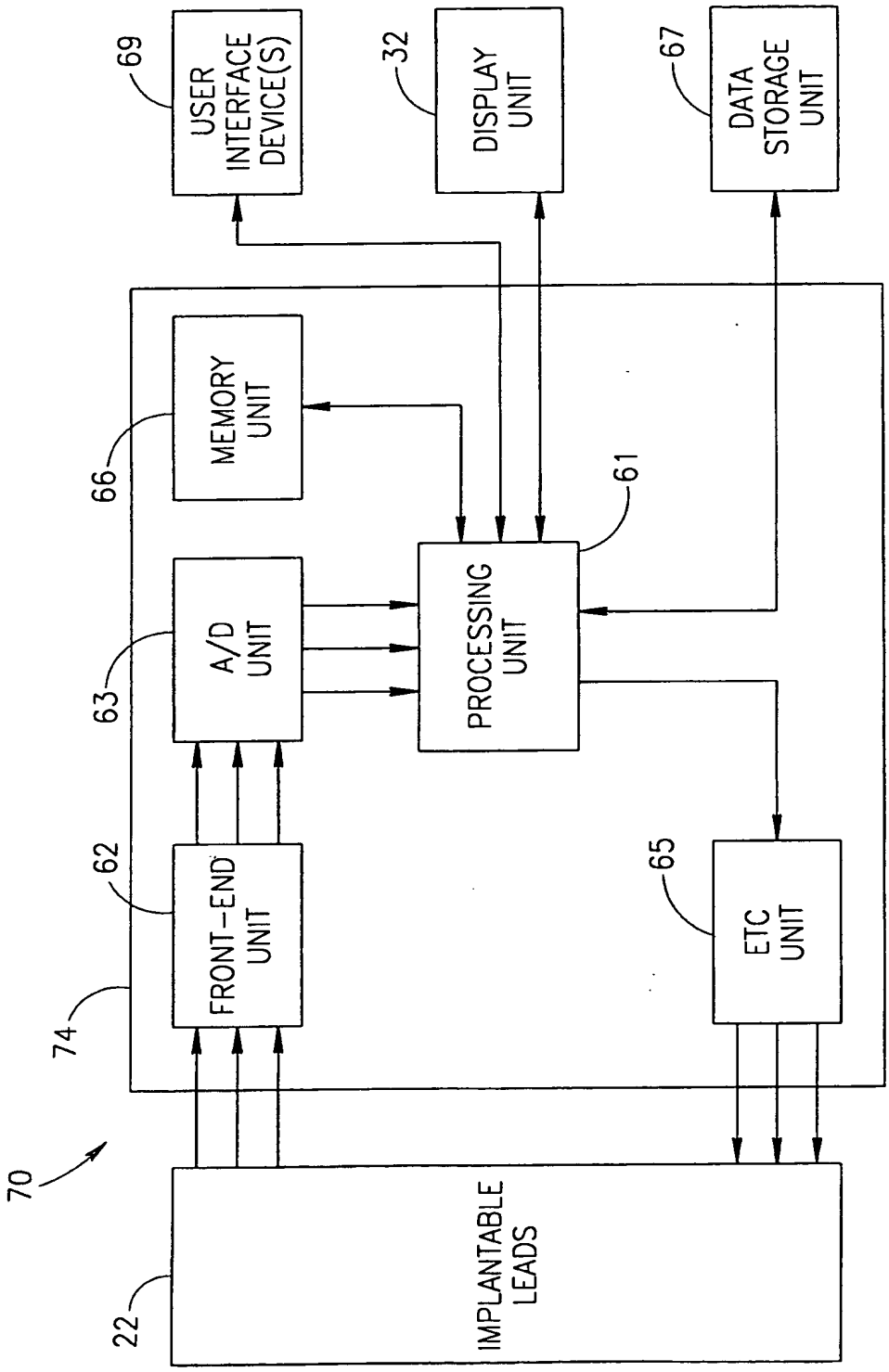

69
USER INTERFACE DEVICE(S)
32
DISPLAY UNIT
67
DATA STORAGE UNIT
66
MEMORY UNIT
61
PROCESSING UNIT
63
A/D UNIT
62
FRONT-END UNIT
65
ETC UNIT
74
70
22
IMPLANTABLE LEADS

FIG.6

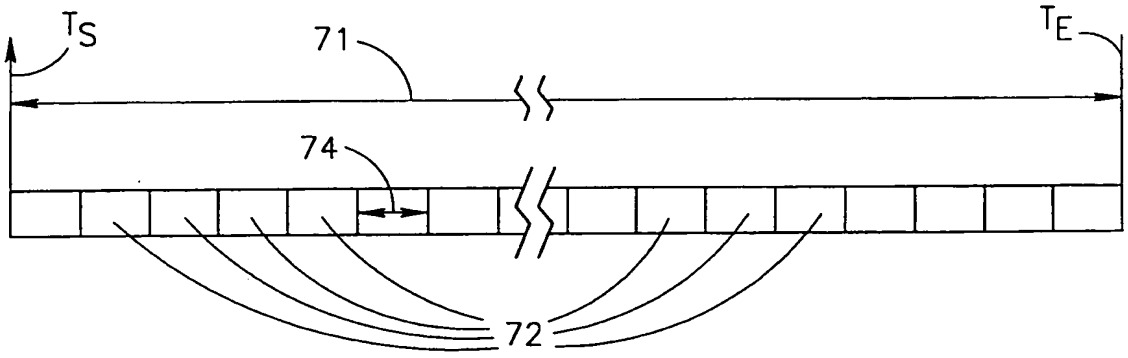

TS
71
TE
74
72

FIG.7

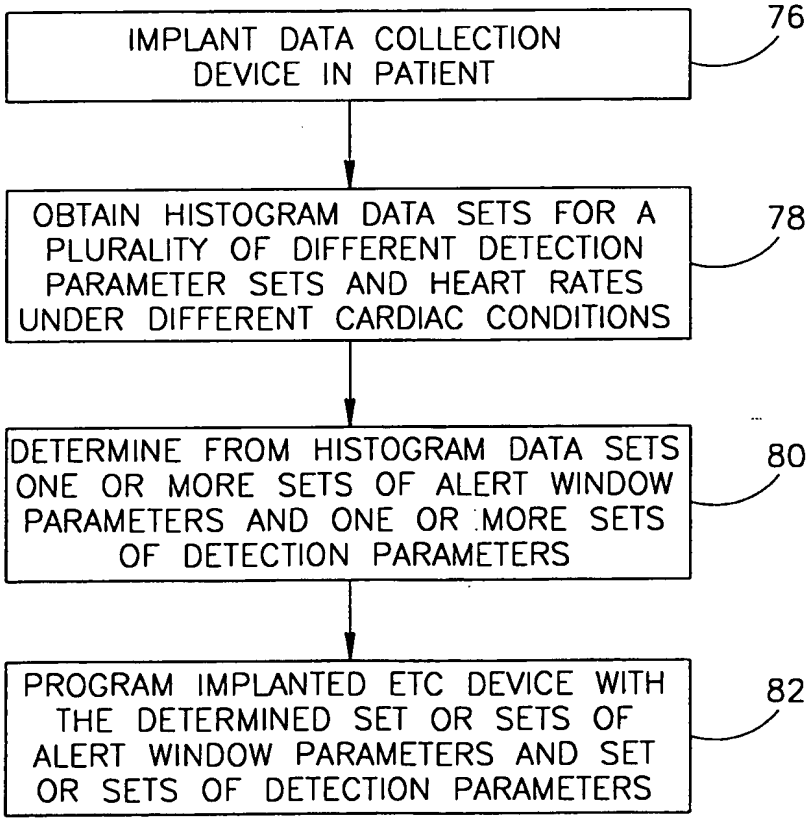
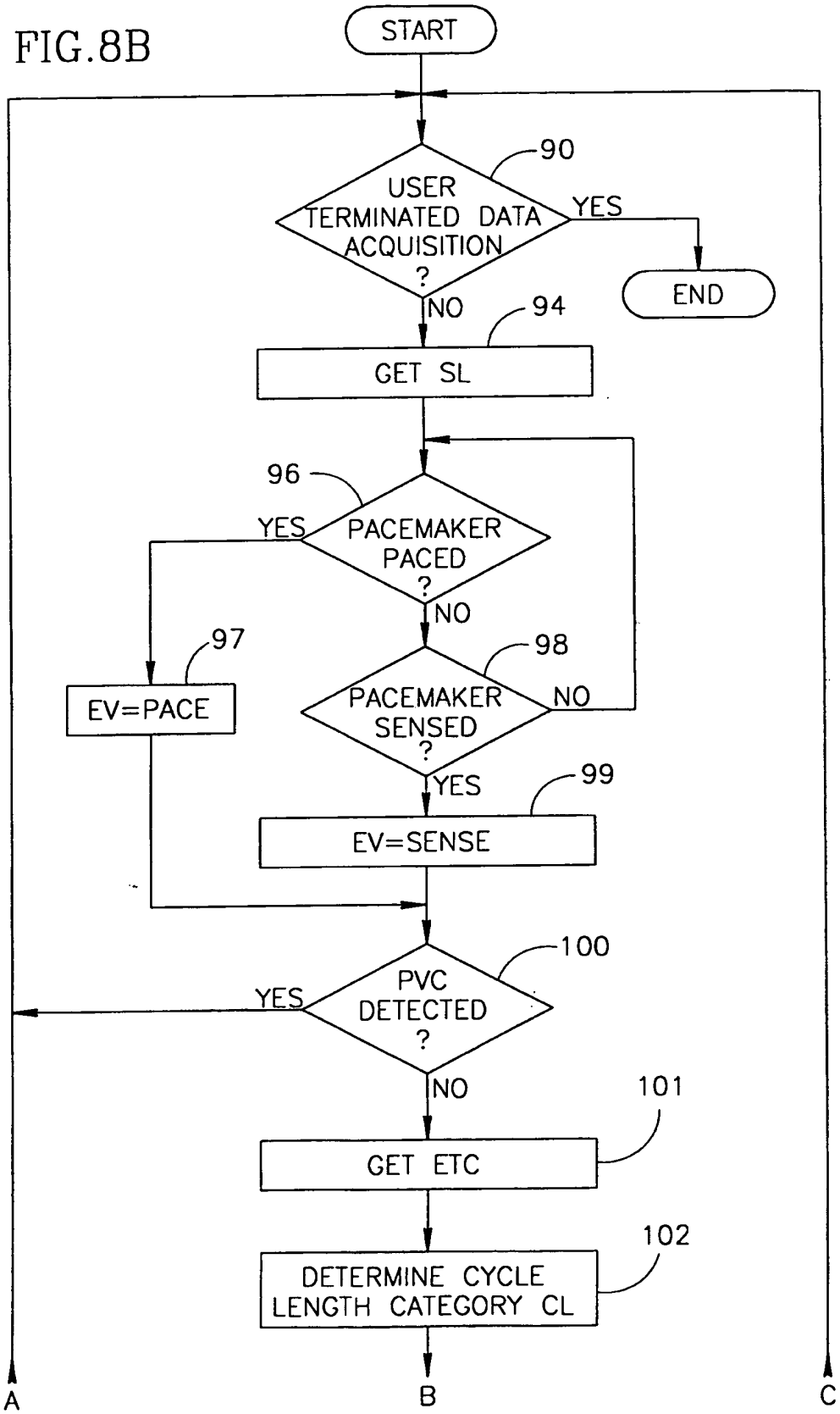

IMPLANT DATA COLLECTION DEVICE IN PATIENT
76
OBTAIN HISTOGRAM DATA SETS FOR A PLURALITY OF DIFFERENT DETECTION PARAMETER SETS AND HEART RATES UNDER DIFFERENT CARDIAC CONDITIONS
78
DETERMINE FROM HISTOGRAM DATA SETS ONE OR MORE SETS OF ALERT WINDOW PARAMETERS AND ONE OR MORE SETS OF DETECTION PARAMETERS
80
PROGRAM IMPLANTED ETC DEVICE WITH THE DETERMINED SET OR SETS OF ALERT WINDOW PARAMETERS AND SET OR SETS OF DETECTION PARAMETERS
82

FIG.8A

FIG.8B


START
90
USER TERMINATED DATA ACQUISITION ?
YES
END
NO
94
GET SL
96
PACEMAKER PACED ?
YES
NO
97
EV=PACE
98
PACEMAKER SENSED ?
NO
YES
99
EV=SENSE
100
PVC DETECTED ?
YES
NO
101
GET ETC
102
DETERMINE CYCLE LENGTH CATEGORY CL
A
B
C

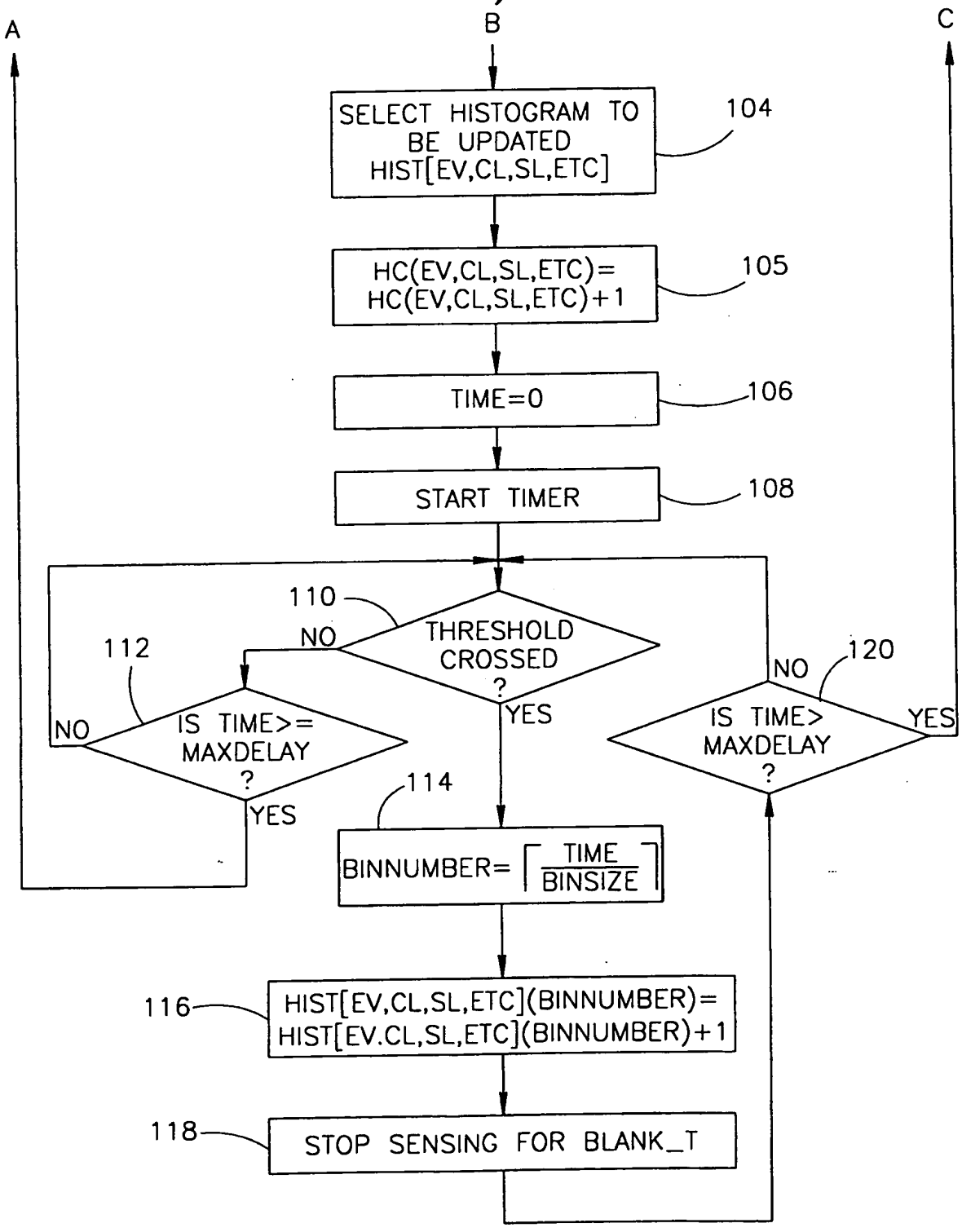

A
B
C
SELECT HISTOGRAM TO BE UPDATED HIST[EV,CL,SL,ETC]
104
HC(EV,CL,SL,ETC)= HC(EV,CL,SL,ETC)+1
105
TIME=0
106
START TIMER
108
110
THRESHOLD CROSSED ?
NO
YES
112
IS TIME>= MAXDELAY ?
NO
YES
120
IS TIME> MAXDELAY ?
NO
YES
114
BINNUMBER= ⌈TIME/BINSIZE⌉
116
HIST[EV,CL,SL,ETC](BINNUMBER)= HIST[EV.CL,SL,ETC](BINNUMBER)+1
118
STOP SENSING FOR BLANK_T

FIG.8C

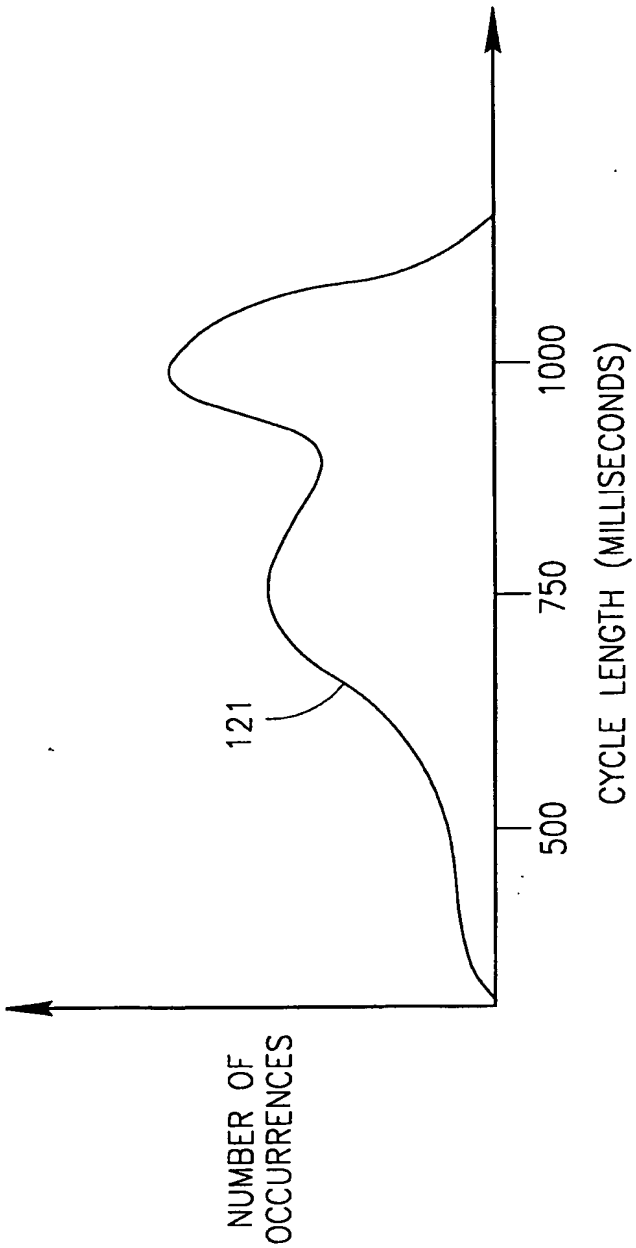



FIG.9
PRIOR ART

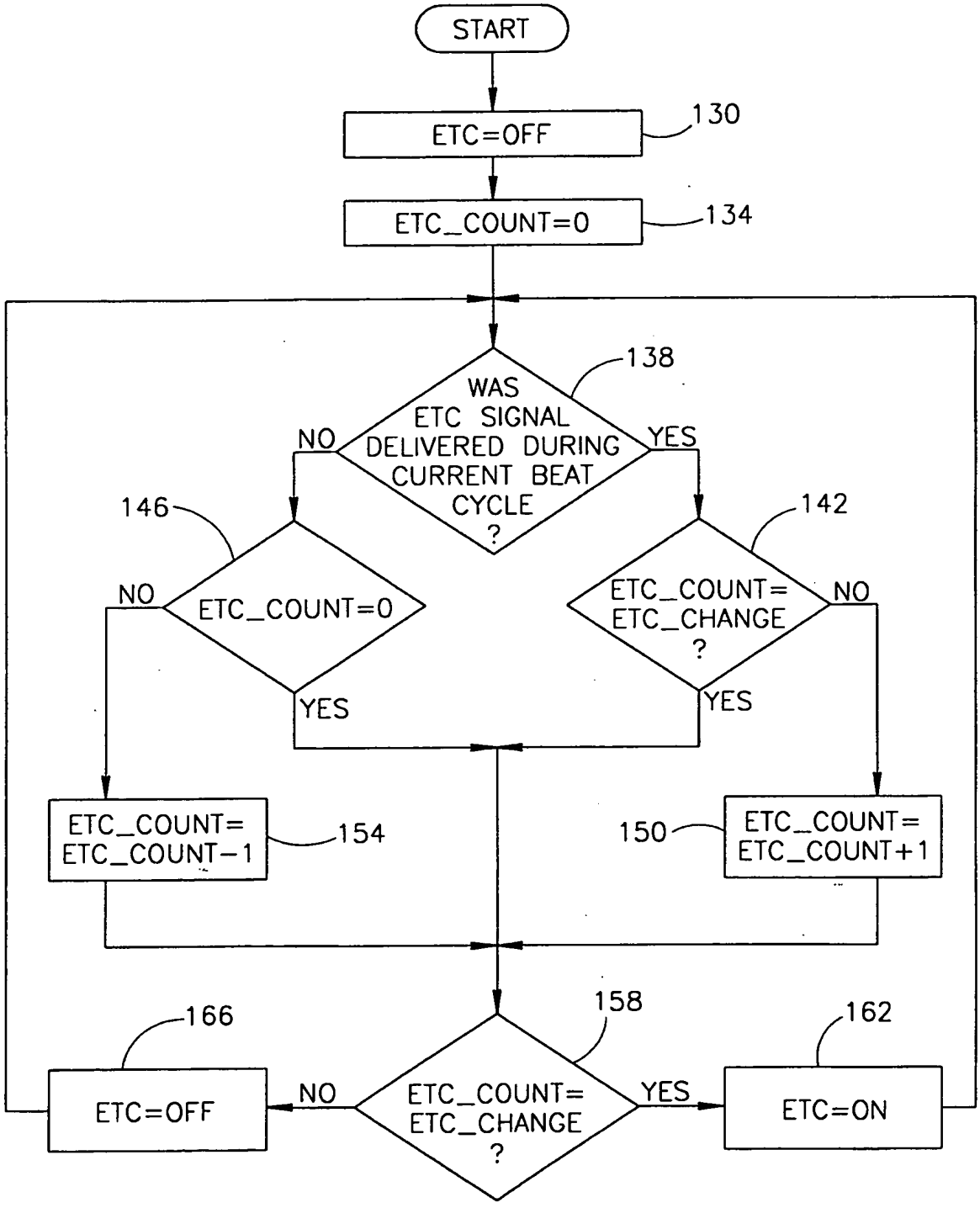

START
ETC=OFF
130
ETC_COUNT=0
134
WAS ETC SIGNAL DELIVERED DURING CURRENT BEAT CYCLE ?
138
NO
YES
146
ETC_COUNT=0
NO
YES
142
ETC_COUNT= ETC_CHANGE ?
NO
YES
ETC_COUNT= ETC_COUNT-1
154
150
ETC_COUNT= ETC_COUNT+1
158
ETC_COUNT= ETC_CHANGE ?
NO
YES
166
ETC=OFF
162
ETC=ON

FIG.10

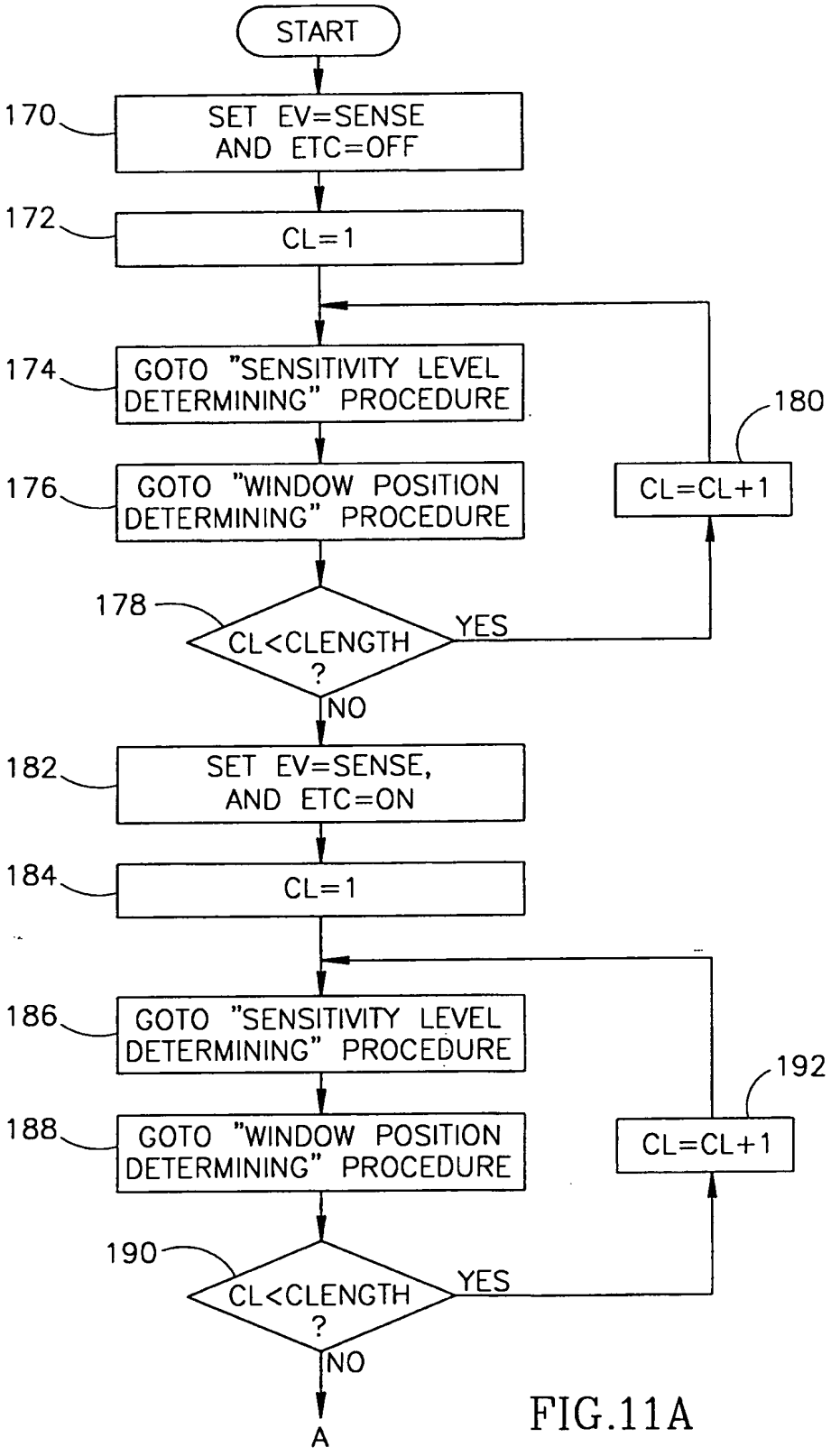

START
170
SET EV=SENSE AND ETC=OFF
172
CL=1
174
GOTO "SENSITIVITY LEVEL DETERMINING" PROCEDURE
176
GOTO "WINDOW POSITION DETERMINING" PROCEDURE
178
CL<CLENGTH ?
YES
NO
180
CL=CL+1
182
SET EV=SENSE, AND ETC=ON
184
CL=1
186
GOTO "SENSITIVITY LEVEL DETERMINING" PROCEDURE
188
GOTO "WINDOW POSITION DETERMINING" PROCEDURE
190
CL<CLENGTH ?
YES
NO
192
CL=CL+1
A

FIG.11A

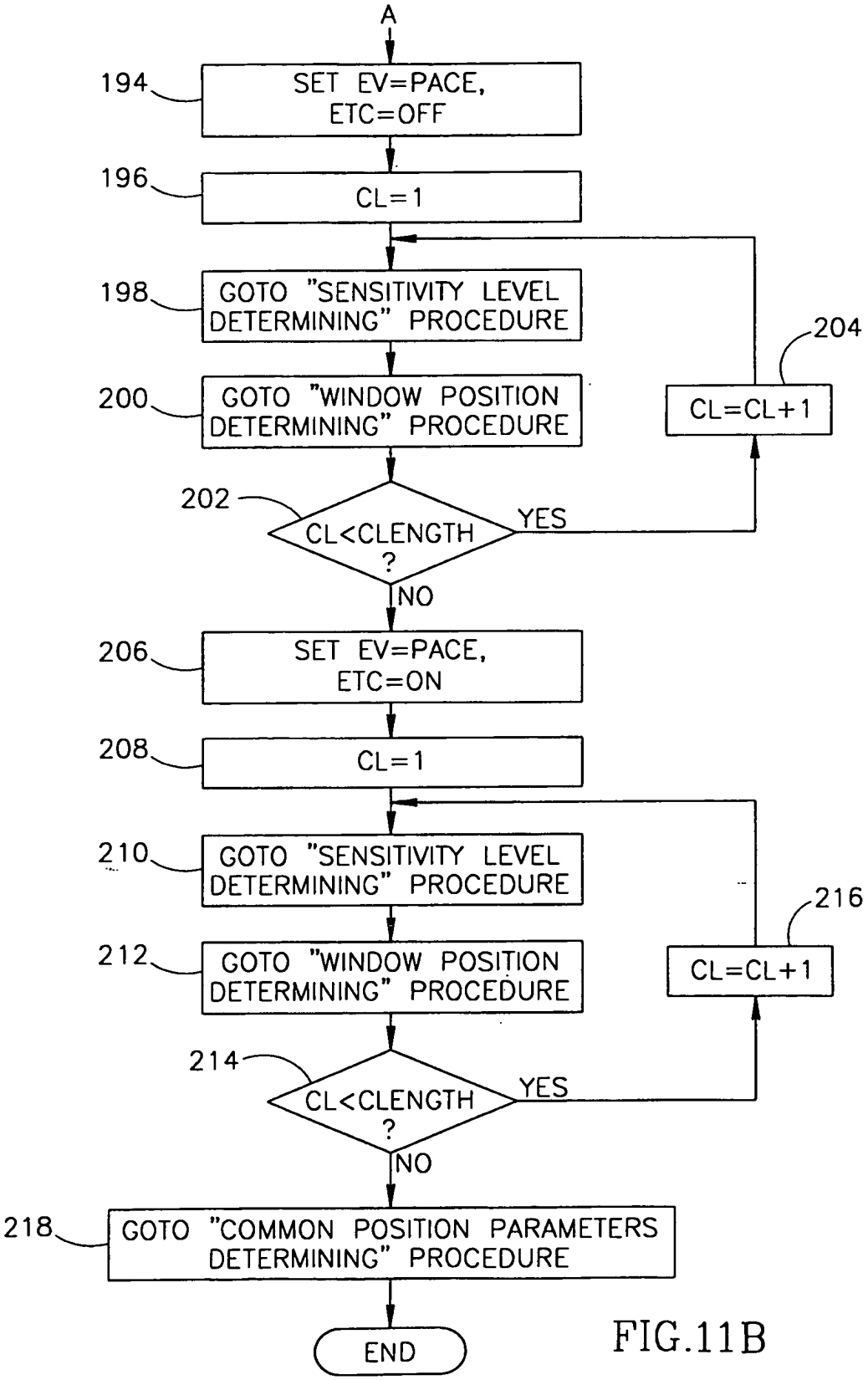

A
194
SET EV=PACE, ETC=OFF
196
CL=1
198
GOTO "SENSITIVITY LEVEL DETERMINING" PROCEDURE
200
GOTO "WINDOW POSITION DETERMINING" PROCEDURE
202
CL<CLENGTH ?
YES
NO
204
CL=CL+1
206
SET EV=PACE, ETC=ON
208
CL=1
210
GOTO "SENSITIVITY LEVEL DETERMINING" PROCEDURE
212
GOTO "WINDOW POSITION DETERMINING" PROCEDURE
214
CL<CLENGTH ?
YES
NO
216
CL=CL+1
218
GOTO "COMMON POSITION PARAMETERS DETERMINING" PROCEDURE
END

FIG.11B

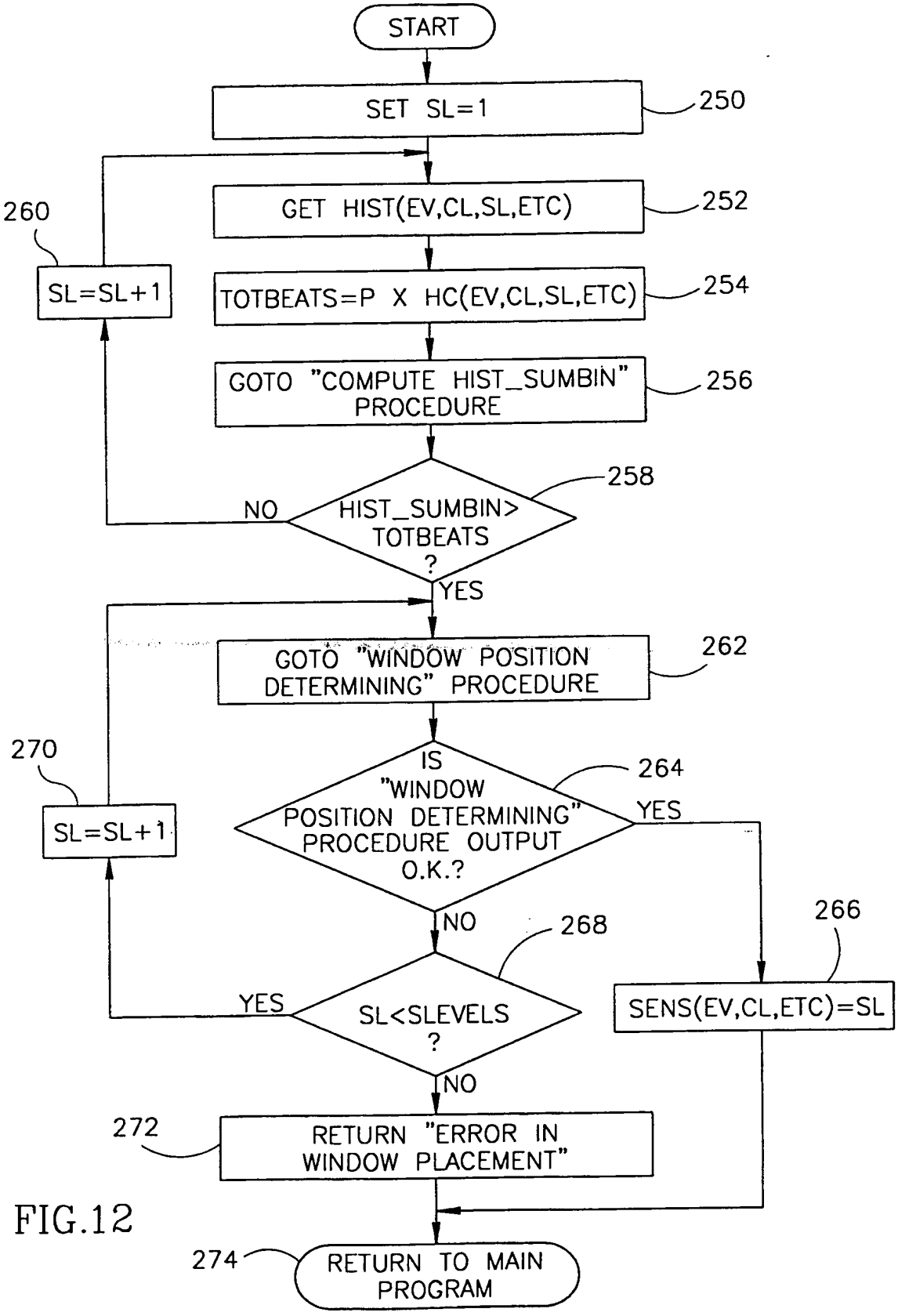

START
SET SL=1
250
GET HIST(EV,CL,SL,ETC)
252
TOTBEATS=P X HC(EV,CL,SL,ETC)
254
GOTO "COMPUTE HIST_SUMBIN" PROCEDURE
256
HIST_SUMBIN> TOTBEATS ?
258
NO
YES
260
SL=SL+1
GOTO "WINDOW POSITION DETERMINING" PROCEDURE
262
IS "WINDOW POSITION DETERMINING" PROCEDURE OUTPUT O.K.?
264
YES
NO
270
SL=SL+1
SL<SLEVELS ?
268
YES
NO
266
SENS(EV,CL,ETC)=SL
272
RETURN "ERROR IN WINDOW PLACEMENT"
274
RETURN TO MAIN PROGRAM

FIG.12

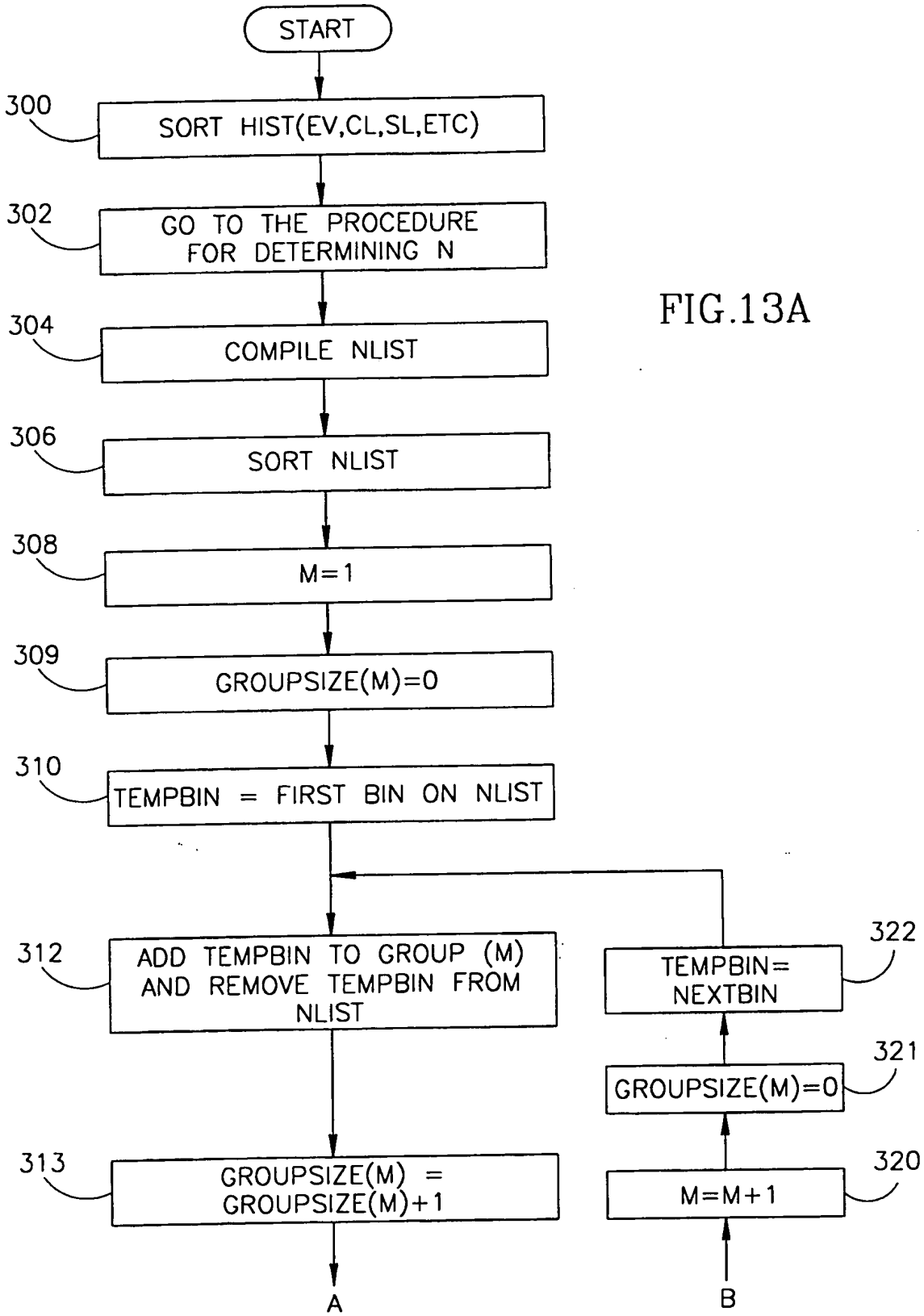

START
300
SORT HIST(EV,CL,SL,ETC)
302
GO TO THE PROCEDURE FOR DETERMINING N
304
COMPILE NLIST
306
SORT NLIST
308
M=1
309
GROUPSIZE(M)=0
310
TEMPBIN = FIRST BIN ON NLIST
312
ADD TEMPBIN TO GROUP (M) AND REMOVE TEMPBIN FROM NLIST
313
GROUPSIZE(M) = GROUPSIZE(M)+1
A
322
TEMPBIN= NEXTBIN
321
GROUPSIZE(M)=0
320
M=M+1
B

FIG.13A

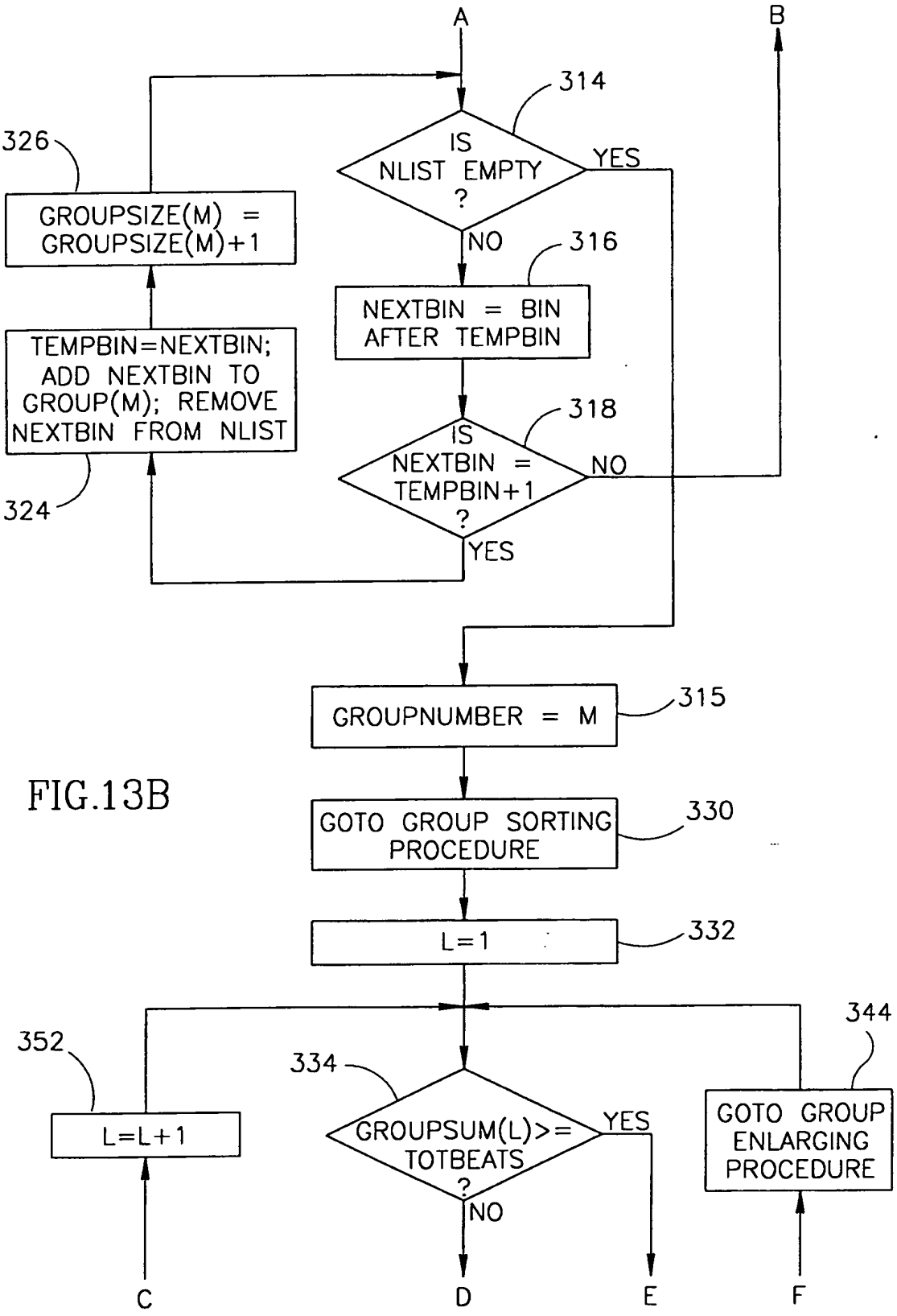

A
B
314
IS NLIST EMPTY ?
YES
NO
316
NEXTBIN = BIN AFTER TEMPBIN
318
IS NEXTBIN = TEMPBIN+1 ?
NO
YES
326
GROUPSIZE(M) = GROUPSIZE(M)+1
TEMPBIN=NEXTBIN; ADD NEXTBIN TO GROUP(M); REMOVE NEXTBIN FROM NLIST
324
GROUPNUMBER = M
315
GOTO GROUP SORTING PROCEDURE
330
L=1
332
352
L=L+1
334
GROUPSUM(L)>= TOTBEATS ?
YES
NO
344
GOTO GROUP ENLARGING PROCEDURE
C
D
E
F

FIG.13B

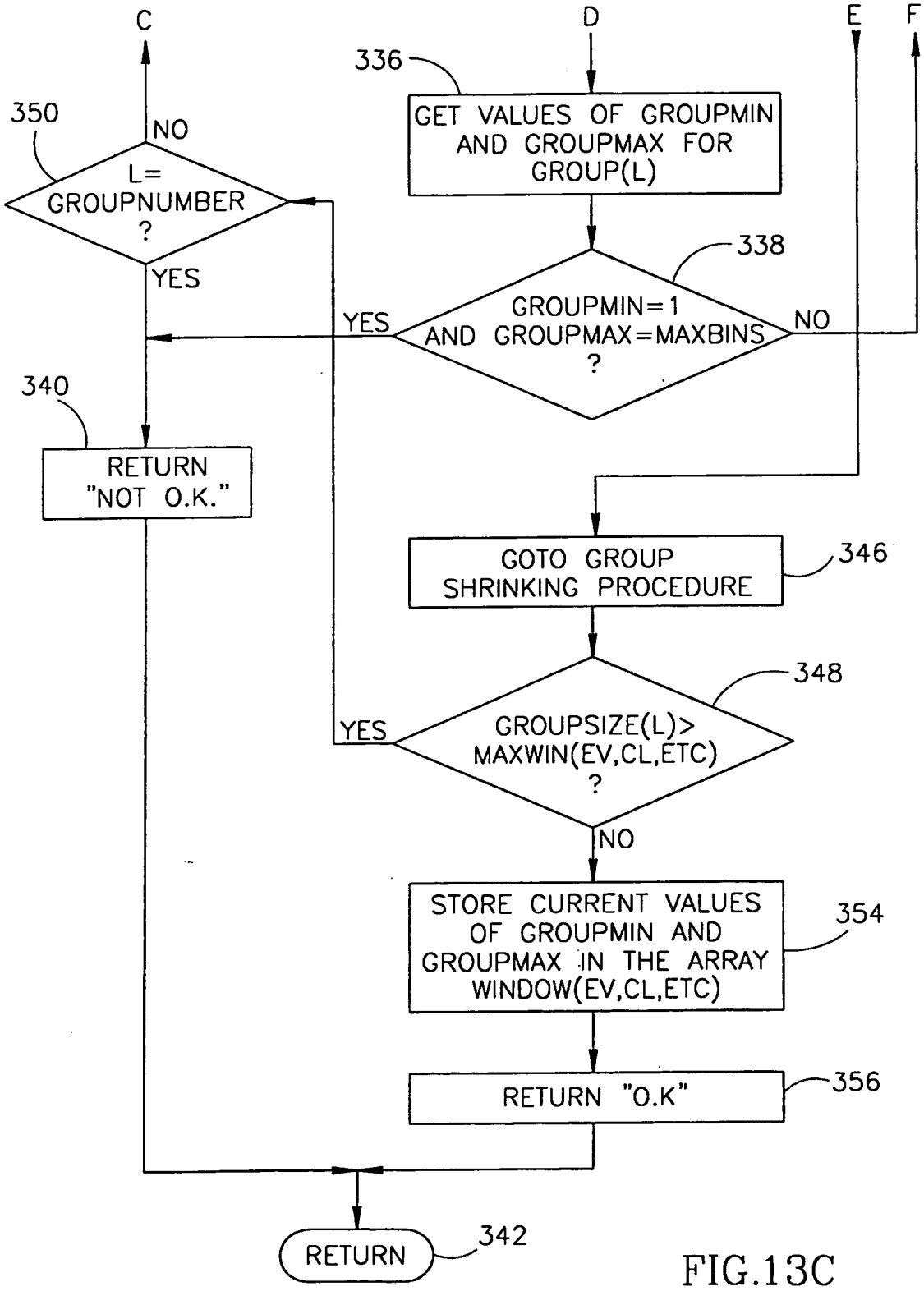

C
D
E
F
336
GET VALUES OF GROUPMIN AND GROUPMAX FOR GROUP(L)
350
NO
L= GROUPNUMBER ?
YES
338
YES
GROUPMIN=1 AND GROUPMAX=MAXBINS ?
NO
340
RETURN "NOT O.K."
GOTO GROUP SHRINKING PROCEDURE
346
348
YES
GROUPSIZE(L)> MAXWIN(EV,CL,ETC) ?
NO
STORE CURRENT VALUES OF GROUPMIN AND GROUPMAX IN THE ARRAY WINDOW(EV,CL,ETC)
354
RETURN "O.K"
356
RETURN
342

FIG.13C

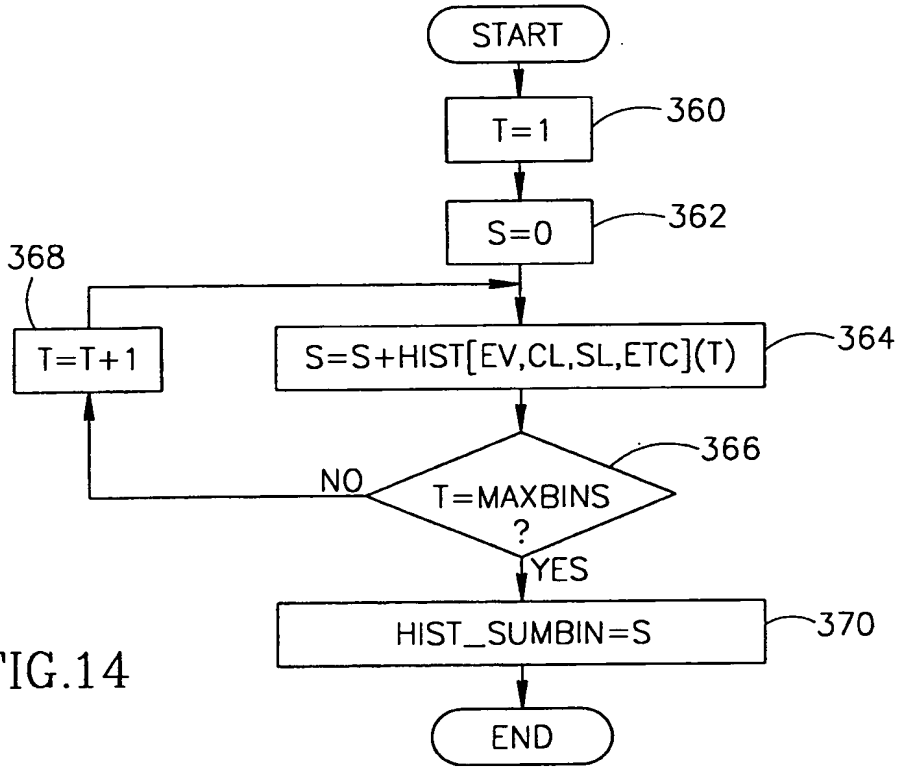

START
T=1
360
S=0
362
368
T=T+1
S=S+HIST[EV,CL,SL,ETC](T)
364
366
NO
T=MAXBINS
?
YES
HIST_SUMBIN=S
370
END

FIG.14

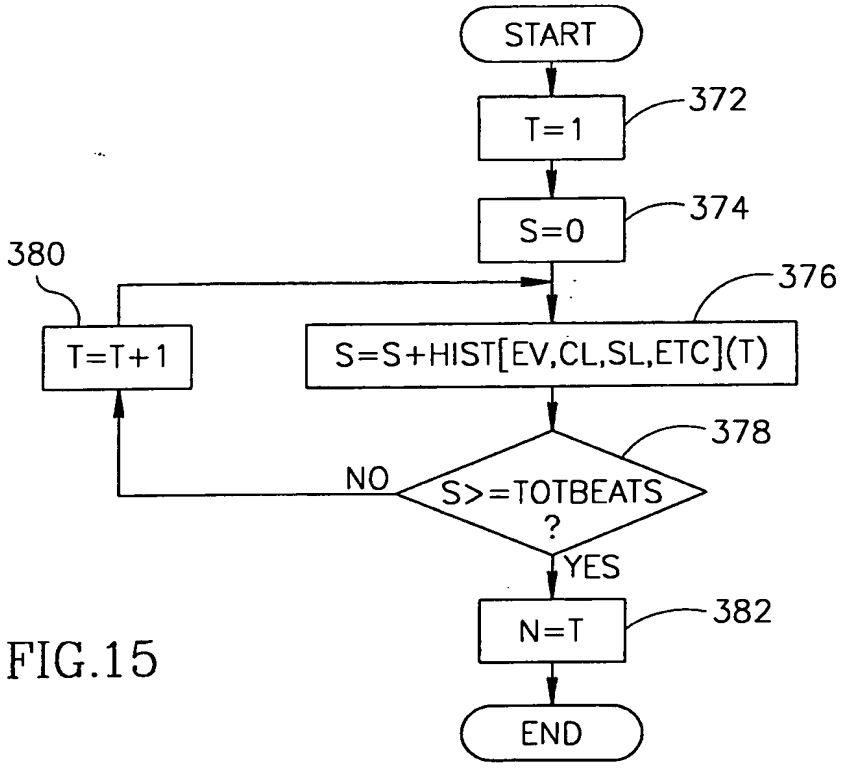

START
T=1
372
S=0
374
380
376
T=T+1
S=S+HIST[EV,CL,SL,ETC](T)
378
NO
S>=TOTBEATS
?
YES
N=T
382
END

FIG.15

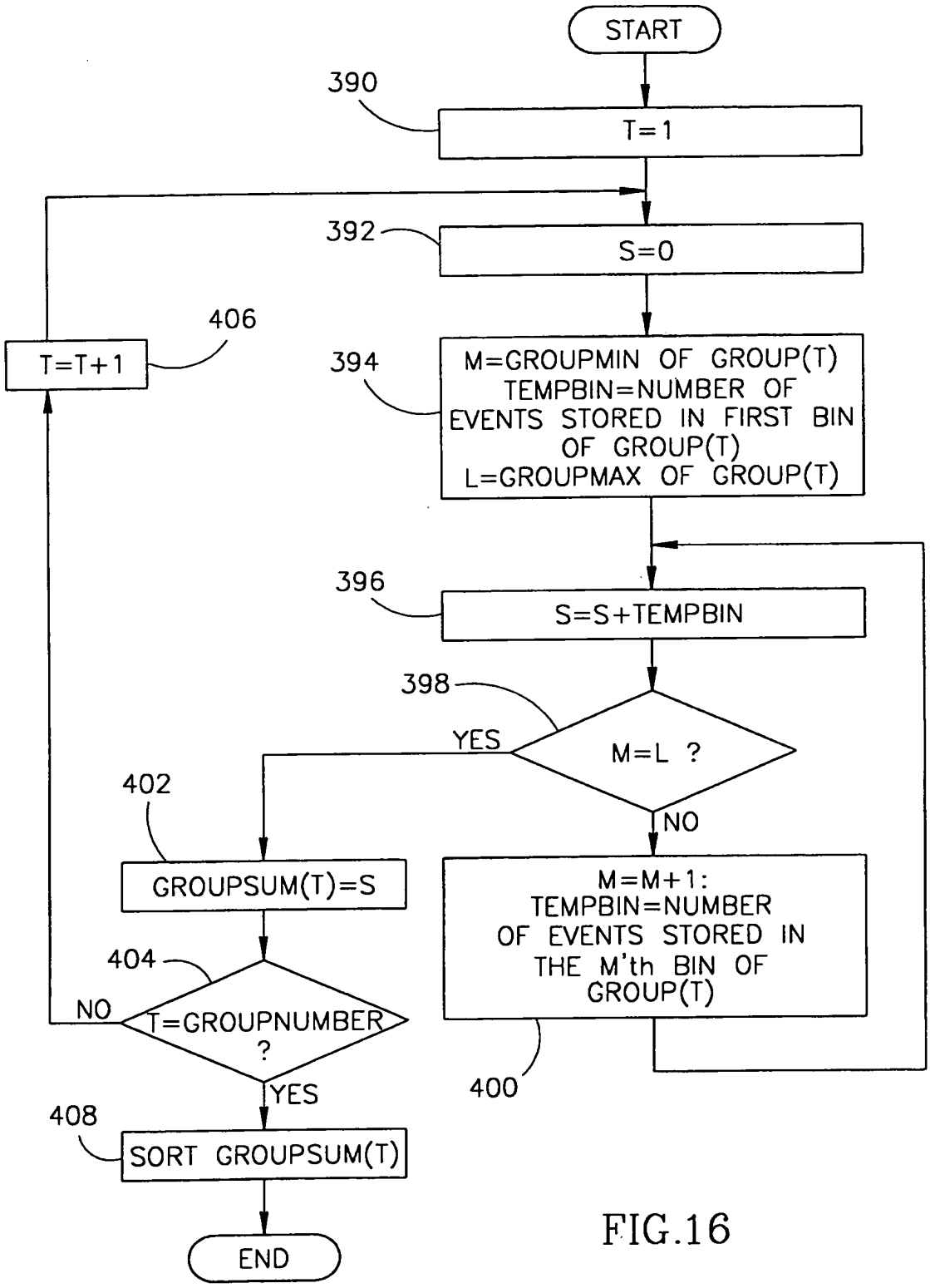

START
390
T=1
392
S=0
406
T=T+1
394
M=GROUPMIN OF GROUP(T)
TEMPBIN=NUMBER OF EVENTS STORED IN FIRST BIN OF GROUP(T)
L=GROUPMAX OF GROUP(T)
396
S=S+TEMPBIN
398
M=L ?
YES
NO
402
GROUPSUM(T)=S
M=M+1:
TEMPBIN=NUMBER OF EVENTS STORED IN THE M'th BIN OF GROUP(T)
400
404
NO
T=GROUPNUMBER ?
YES
408
SORT GROUPSUM(T)
END

FIG.16

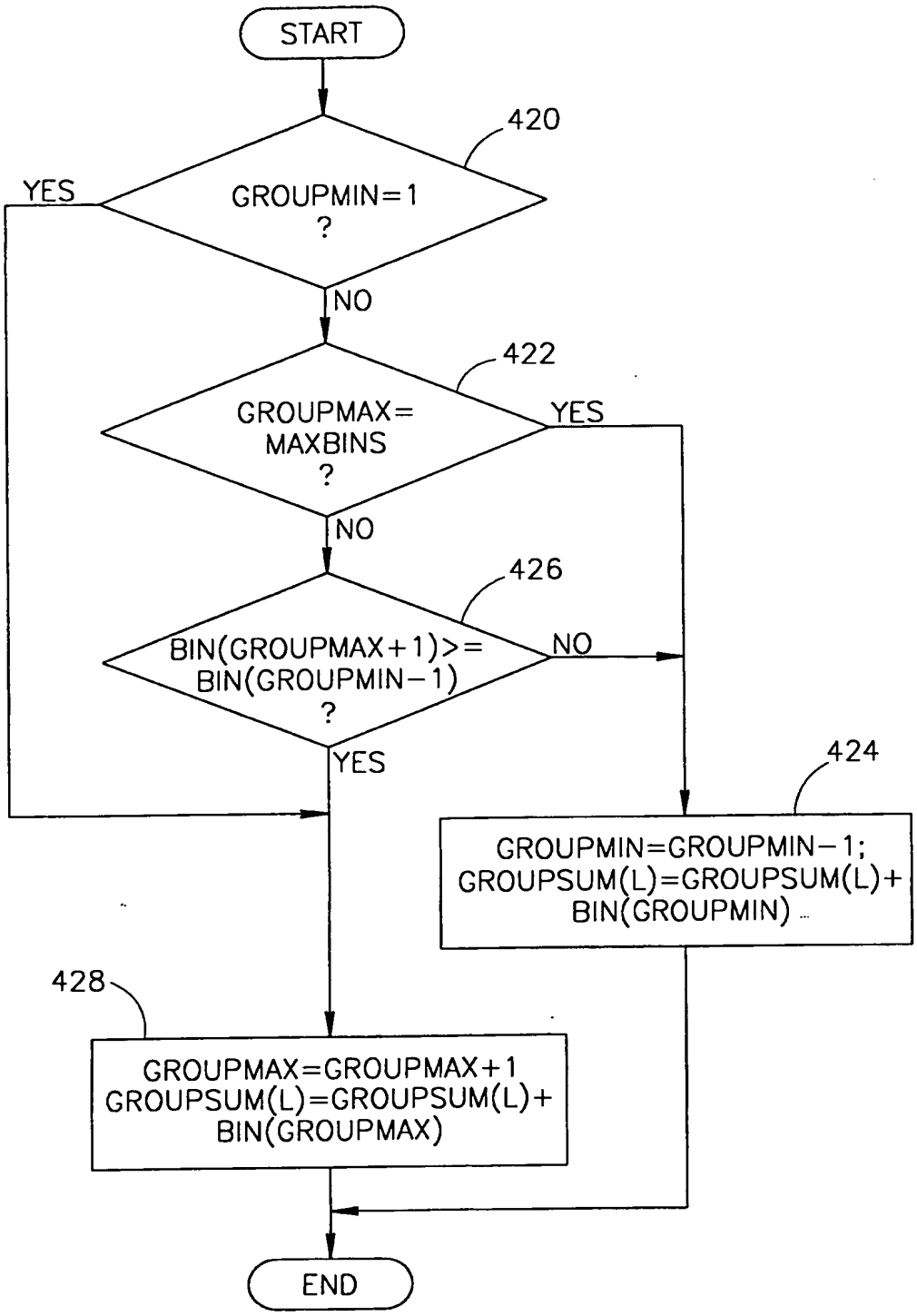

START
420
GROUPMIN=1
?
YES
NO
422
GROUPMAX=
MAXBINS
?
YES
NO
426
BIN(GROUPMAX+1)>=
BIN(GROUPMIN-1)
?
NO
YES
424
GROUPMIN=GROUPMIN-1;
GROUPSUM(L)=GROUPSUM(L)+
BIN(GROUPMIN)
428
GROUPMAX=GROUPMAX+1
GROUPSUM(L)=GROUPSUM(L)+
BIN(GROUPMAX)
END

FIG.17

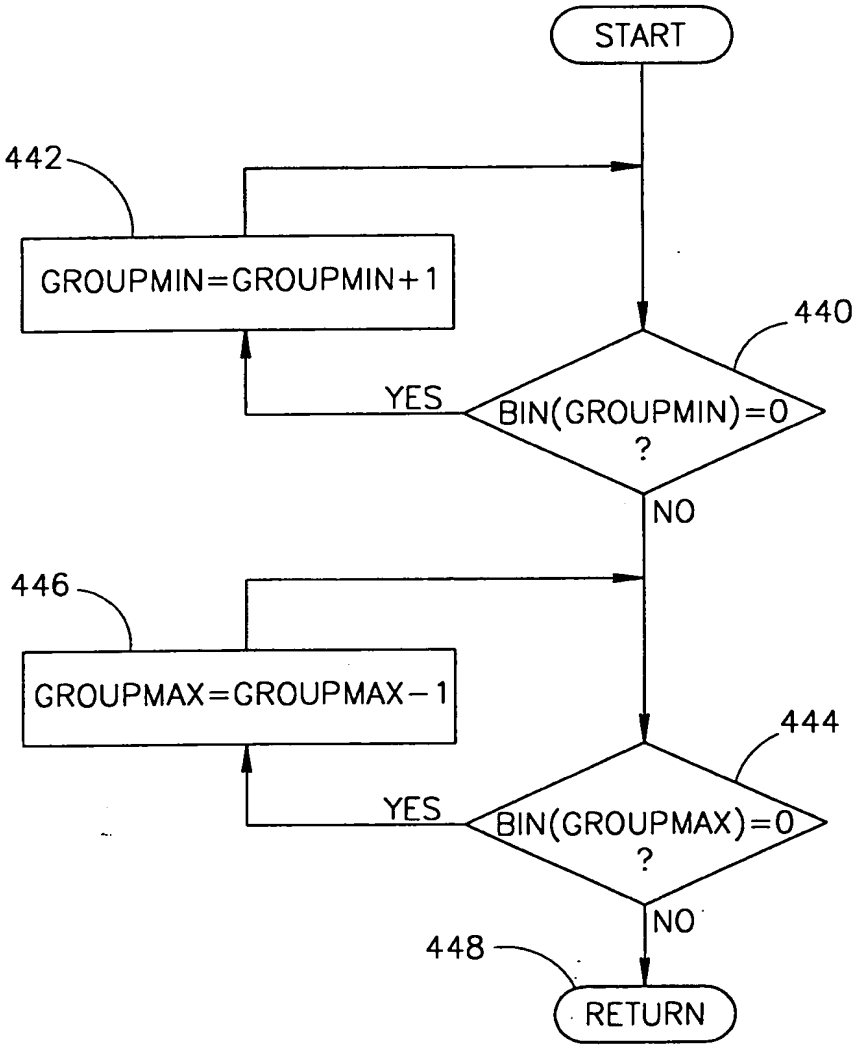

START
442
GROUPMIN=GROUPMIN+1
440
YES
BIN(GROUPMIN)=0
?
NO
446
GROUPMAX=GROUPMAX-1
444
YES
BIN(GROUPMAX)=0
?
NO
448
RETURN

FIG.18

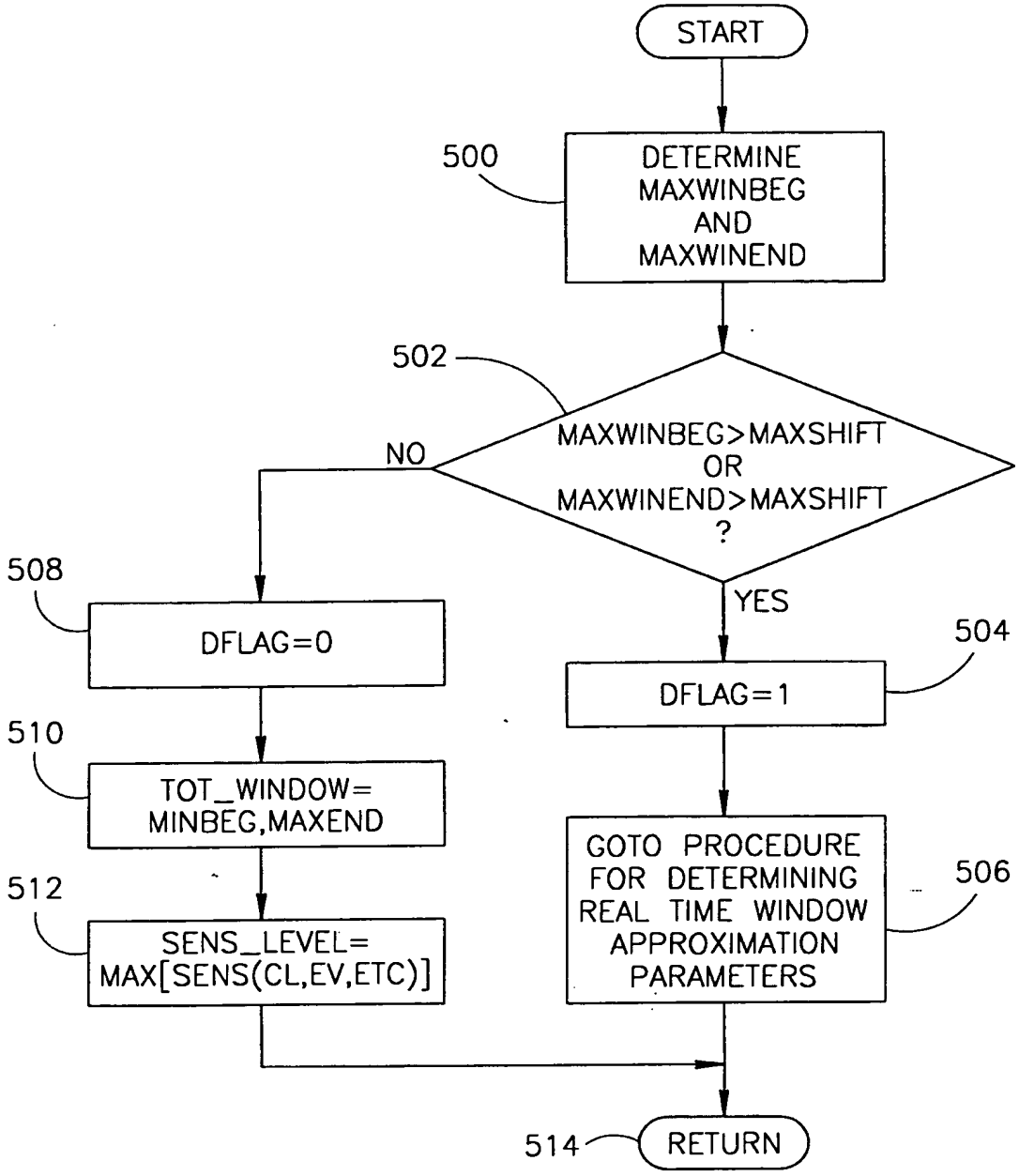

START
500
DETERMINE MAXWINBEG AND MAXWINEND
502
MAXWINBEG>MAXSHIFT OR MAXWINEND>MAXSHIFT ?
NO
YES
508
DFLAG=0
504
DFLAG=1
510
TOT_WINDOW= MINBEG,MAXEND
512
SENS_LEVEL= MAX[SENS(CL,EV,ETC)]
GOTO PROCEDURE FOR DETERMINING REAL TIME WINDOW APPROXIMATION PARAMETERS
506
514
RETURN

FIG.19

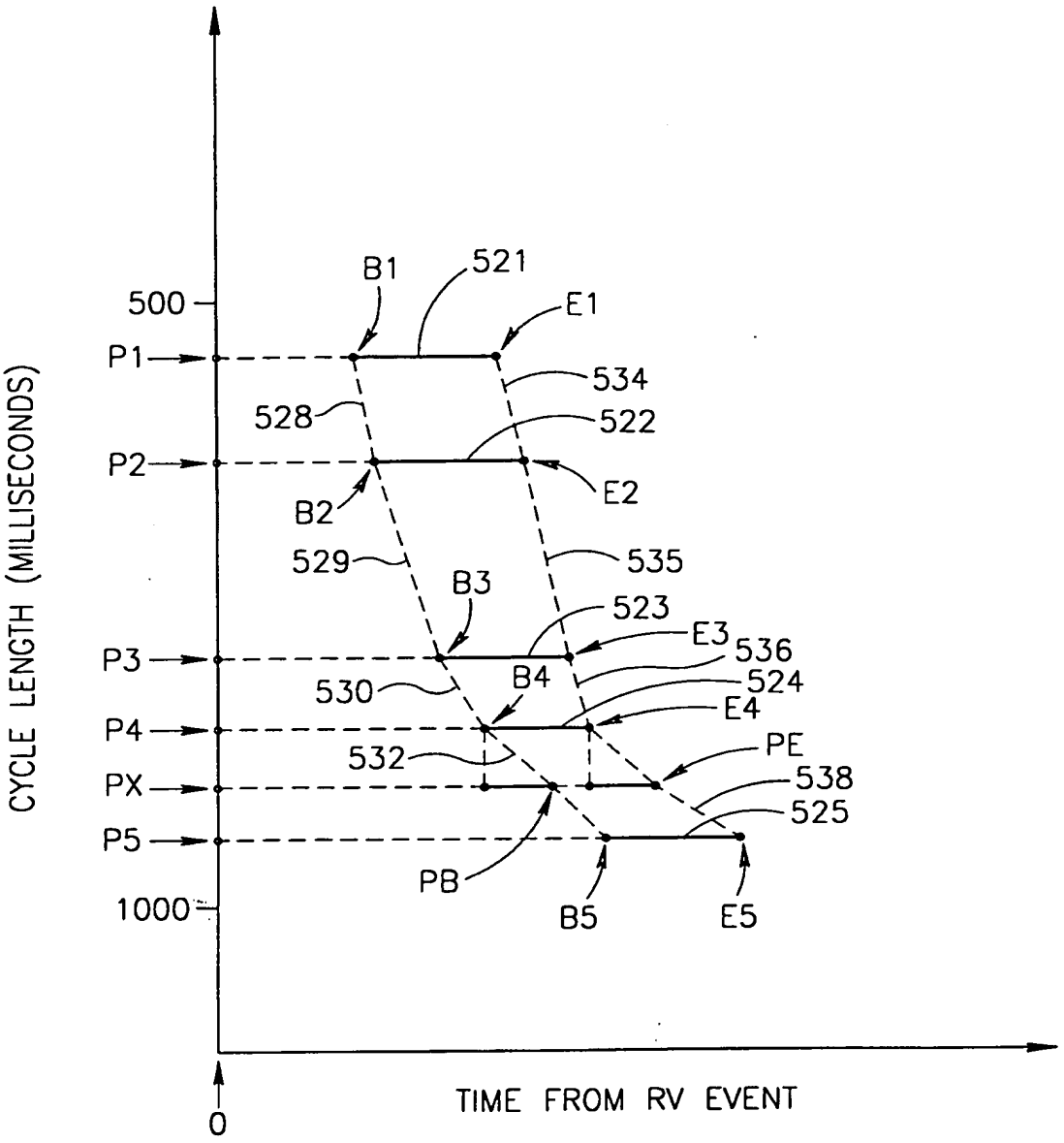

CYCLE LENGTH (MILLISECONDS)
500
1000
P1
P2
P3
P4
PX
P5
0
B1
521
E1
534
528
522
E2
B2
529
535
B3
523
E3
536
530
B4
524
E4
532
PE
538
525
PB
B5
E5
TIME FROM RV EVENT

FIG.20

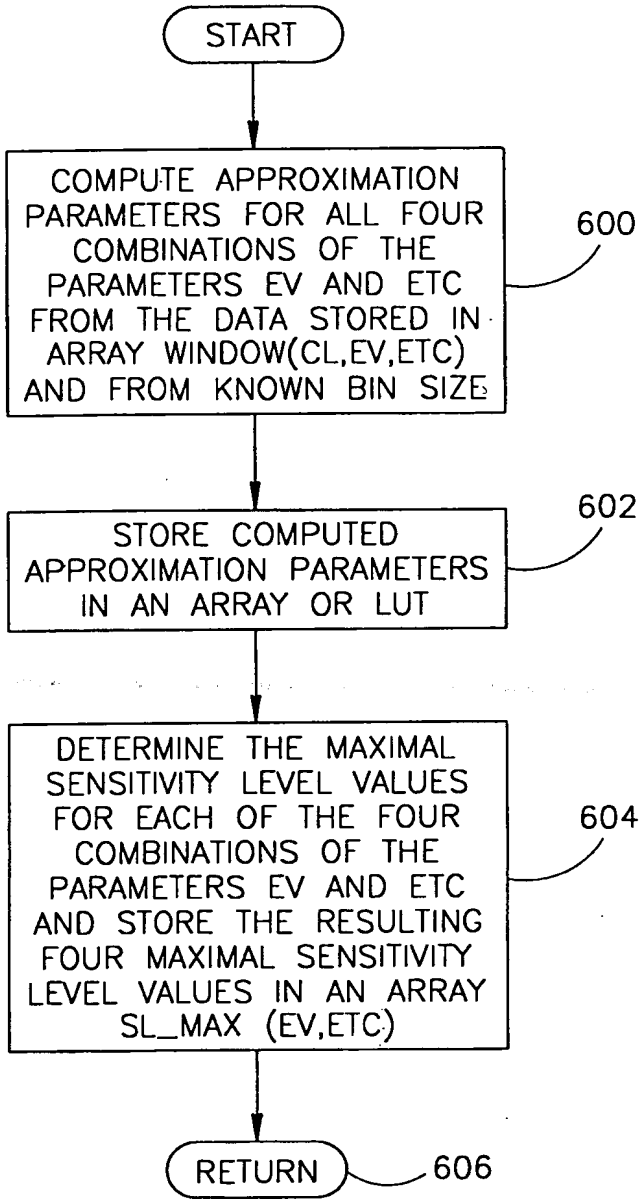

START
COMPUTE APPROXIMATION PARAMETERS FOR ALL FOUR COMBINATIONS OF THE PARAMETERS EV AND ETC FROM THE DATA STORED IN ARRAY WINDOW(CL,EV,ETC) AND FROM KNOWN BIN SIZE
600
STORE COMPUTED APPROXIMATION PARAMETERS IN AN ARRAY OR LUT
602
DETERMINE THE MAXIMAL SENSITIVITY LEVEL VALUES FOR EACH OF THE FOUR COMBINATIONS OF THE PARAMETERS EV AND ETC AND STORE THE RESULTING FOUR MAXIMAL SENSITIVITY LEVEL VALUES IN AN ARRAY SL_MAX (EV,ETC)
604
RETURN
606

FIG.21

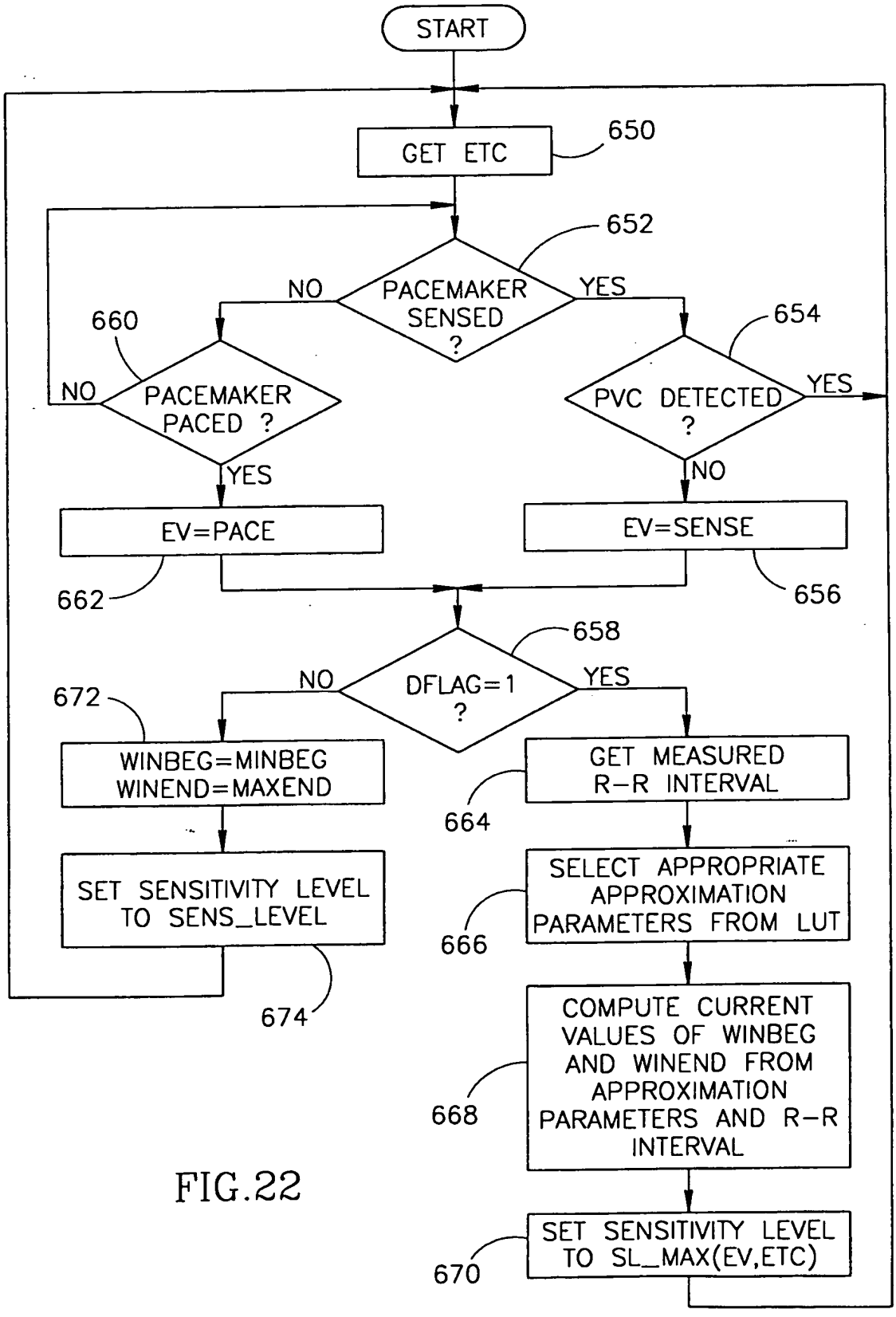
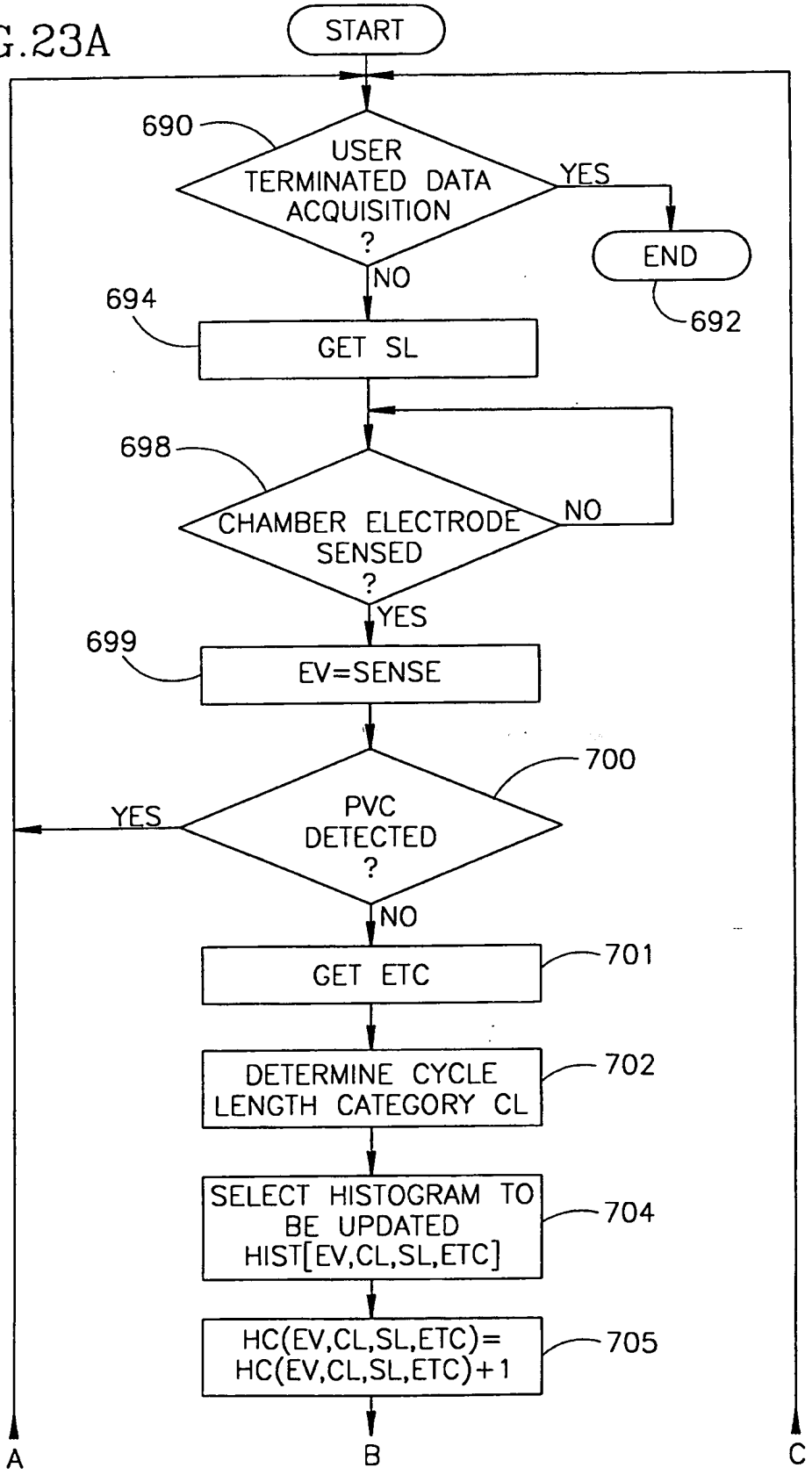

START
GET ETC
650
652
PACEMAKER SENSED ?
NO
YES
660
PACEMAKER PACED ?
NO
YES
654
PVC DETECTED ?
YES
NO
EV=PACE
662
EV=SENSE
656
658
DFLAG=1 ?
NO
YES
672
WINBEG=MINBEG
WINEND=MAXEND
SET SENSITIVITY LEVEL TO SENS_LEVEL
674
GET MEASURED R-R INTERVAL
664
SELECT APPROPRIATE APPROXIMATION PARAMETERS FROM LUT
666
COMPUTE CURRENT VALUES OF WINBEG AND WINEND FROM APPROXIMATION PARAMETERS AND R-R INTERVAL
668
SET SENSITIVITY LEVEL TO SL_MAX(EV,ETC)
670

FIG.22

FIG.23A


START
690
USER TERMINATED DATA ACQUISITION ?
YES
END
692
NO
694
GET SL
698
CHAMBER ELECTRODE SENSED ?
NO
YES
699
EV=SENSE
700
PVC DETECTED ?
YES
NO
701
GET ETC
702
DETERMINE CYCLE LENGTH CATEGORY CL
704
SELECT HISTOGRAM TO BE UPDATED HIST[EV,CL,SL,ETC]
705
HC(EV,CL,SL,ETC)= HC(EV,CL,SL,ETC)+1
A
B
C

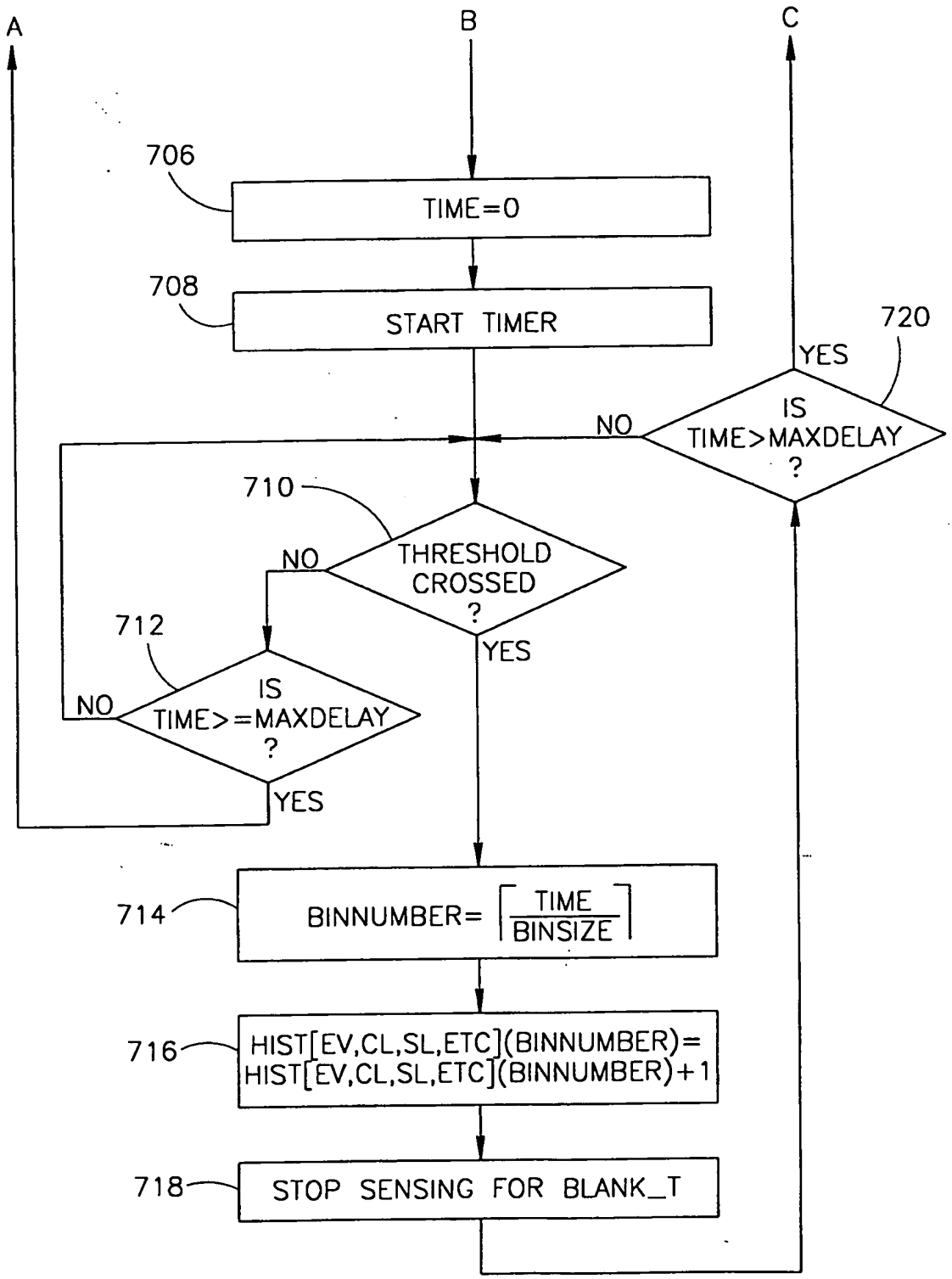

A
B
C
706
TIME=0
708
START TIMER
720
YES
IS
TIME>MAXDELAY
?
NO
710
NO
THRESHOLD
CROSSED
?
YES
712
NO
IS
TIME>=MAXDELAY
?
YES
714
BINNUMBER= ⌈TIME/BINSIZE⌉
716
HIST[EV,CL,SL,ETC](BINNUMBER)=
HIST[EV,CL,SL,ETC](BINNUMBER)+1
718
STOP SENSING FOR BLANK_T

FIG.23B

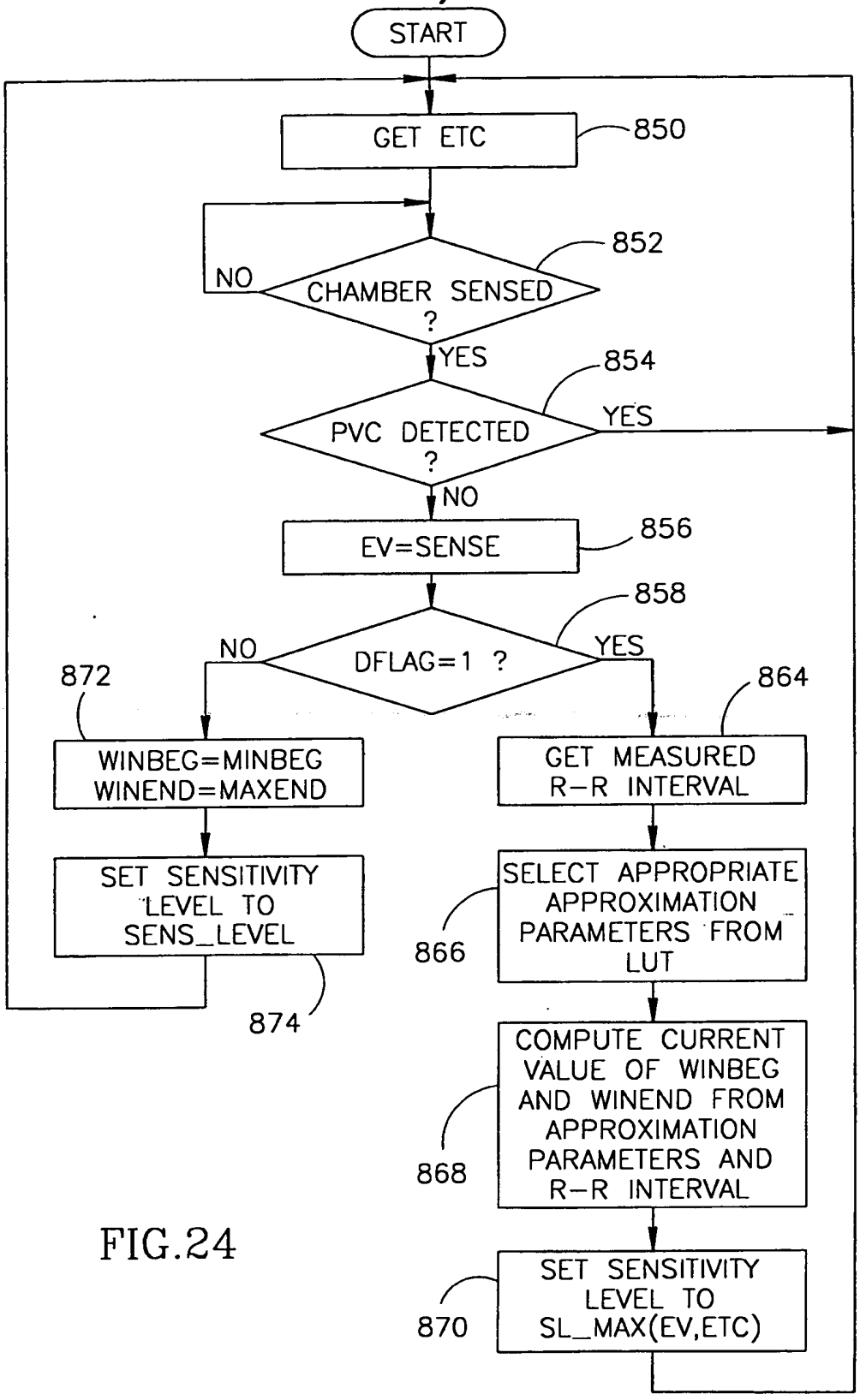

START
GET ETC
850
852
NO
CHAMBER SENSED ?
YES
854
PVC DETECTED ?
YES
NO
EV=SENSE
856
858
NO
DFLAG=1 ?
YES
872
WINBEG=MINBEG
WINEND=MAXEND
SET SENSITIVITY LEVEL TO SENS_LEVEL
874
864
GET MEASURED R-R INTERVAL
SELECT APPROPRIATE APPROXIMATION PARAMETERS FROM LUT
866
COMPUTE CURRENT VALUE OF WINBEG AND WINEND FROM APPROXIMATION PARAMETERS AND R-R INTERVAL
868
SET SENSITIVITY LEVEL TO SL_MAX(EV,ETC)
870

FIG.24